

HEALTHY LONGEVITY GLOBAL COMPETITION

2024 Catalyst Awardees

Sponsor: Chinese Academy of Medical Sciences

A New Glioma Drug Target and a Novel Peptide Self-Assembly Drug Delivery System

Principal Investigator	Xinxin Li, PhD
PI Primary Affiliation	Chinese Academy of Medical Science
Co-Investigator(s)	None

PROJECT DESCRIPTION

Glioma is the most common intracranial malignant tumor, with incidence increasing with age. The global aging population has driven a sharp rise in glioma cases, posing a significant threat to human health and longevity. Current therapies, such as surgery and radiotherapy, are often unsuitable for elderly patients due to their invasive nature and severe side effects, highlighting the urgent need for novel therapeutic strategies. This study identifies, for the first time, the d-opioid receptor (DOR) as being overexpressed in tumor sites of both clinical glioma patients and glioma-in-situ mouse models, establishing DOR as a promising drug delivery target. On the one hand, this project aims to develop anti-glioma drugs derived from natural products targeting the DOR. On the other hand, building on our previous discovery of a self-assembling tetrapeptide capable of crossing the blood-brain barrier (BBB), we propose integrating this peptide into a novel dual-targeting drug delivery system. This delivery system could traverse the BBB in a transcytosis pathway mediated by insulin receptor (IR), and then accurately recognize glioma cells by targeting IR and DOR to achieve efficient and precise drug delivery. This project is intended to overcome the lack of effective clinical drug therapies for glioma. This project expects to offer new therapeutic candidates for glioma, particularly in elderly patients, advancing global efforts to improve health and extend longevity.

AI-based Multidimensional Digital Assessment Model of Immunity for the Elderly and Its Applications

Principal Investigator	Guobing Chen, PhD
PI Primary Affiliation	School of Medicine, Jinan University
Co-Investigator(s)	Oscar Junhong Luo, PhD; Chanchan Xiao, PhD; Jun Su, M.M; Wen Gao, PhD; Lipeng Mao, PhD;

PROJECT DESCRIPTION

China faces aging challenges and has set national goals for healthy aging. Aging affects the immune system, increasing disease susceptibility and reducing clearance of senescent cells. The "Immune Age" model uses machine learning on multidimensional immunomics indicators to assess and predict immune age in the elderly. This model helps assess health, predict disease risk, and assist in diagnosis and treatment. It is supported by Jinan University's National Key Laboratory, supercomputing platforms, and the Guangdong-Hong Kong-Macao Greater Bay Area Institute of Geriatric Immunology. The project has conducted extensive research, including immune cell tests and multi-omics sequencing. The model will be applied in Guangzhou Elderly Home and 13 hospitals nationwide for elderly disease research. It aims to establish immune screening areas, promoting practical application and laying the groundwork for future commercial recognition and value.

Antimicrobial coatings for medical catheters associated with intensive care units

Principal Investigator	Yueming Wu, PhD
PI Primary Affiliation	East China University of Science and Technology
Co-Investigator(s)	Runhui Liu, PhD

PROJECT DESCRIPTION

In the intensive care unit (ICU), catheter-induced bacterial colonization and urinary tract infections (UTIs) are critical challenges, exacerbated by the rising issue of antibiotic resistance. Traditional antimicrobial-coated catheters are no longer sufficient to meet clinical demands, necessitating the urgent need for innovative anti-infection strategies to reduce patient complications and enhance care quality.

This research focuses on designing and synthesizing antimicrobial polymers that mimic host defense peptides (HDPs) using ring-opening polymerization. HDPs are promising alternatives to traditional antibiotics due to their broad-spectrum antimicrobial properties and low potential for resistance. However, their poor biostability and high cost limit their practical applications. This project aims to overcome these limitations by developing novel HDP-mimic antimicrobial polymers that maintain the advantages of HDPs while improving stability in physiological environments and cost-effectiveness. We use fast and open-vessel ring-opening polymerization which enables precise control over polymer structure. This ensures that the resulting HDP-mimic polymers exhibit potent antimicrobial activity against drug-resistant bacteria both in vitro and in vivo, while preventing the development of microbial resistance. Additionally, the successful covalent grafting of these antimicrobial polymers onto catheter surfaces has demonstrated significant efficacy against drug-resistant bacteria in laboratory tests and in large animal experiments, laying a solid foundation for clinical translation.

The anticipated outcomes include the development of a highly effective, low-resistance antimicrobial coating for catheters, leading to a significant reduction in catheter-associated UTIs in the ICU. This innovative solution aims to address the global challenge of antibiotic resistance and improve ICU patient safety and outcomes.

Application of Physics-Informed Neural Network and Organoid Vascular Model in Thrombotic Risk Evaluation in Abdominal Aortic Aneurysm

Principal Investigator	Xiaoning SUN, MD
PI Primary Affiliation	Department of Vascular Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College
Co-Investigator(s)	Siting LI, MD; Yuehong ZHENG, MD; Zijian WANG, BS; Zenghan CAO, MD Candidate

PROJECT DESCRIPTION

The incidence rate of abdominal aortic aneurysms is increasing in recent years. Intra-luminal thrombus (ILT) in abdominal aortic aneurysms (AAAs) is associated with aneurysm progression, rupture, and peri-operational embolic complications. Acute in-stent thrombus formation after endovascular aortic repair (EVAR) is a catastrophic threat to the affected limb and/or viscera. Conventionally, the management strategy of AAA is simply based on AAA diameter and/or subjective empirical evaluation of clinicians. Individualized thrombosis assessment are urgently needed to evaluate postoperative outcomes. Computational fluid dynamics (CFD) simulation is capable of individualized assessment of aortic lesions, but due to 1) the complex workflow and tremendous computational burden, and 2) the simulation results yet lack the support of basic experiments, aortic blood-flow simulation has not been widely used in clinical practice. To address the above issues, this project plans to 1) construct a clinical-imaging database of AAA; 2) use physics-informed neural network (PINN) to foster a real-time aortic blood-flow field simulation tool, and to calibrate the model with CFD analysis; 3) apply micro-fluidic vascular microchips to validate the mechanism of thrombus formation under individualized hemodynamic

environment in vitro; (4) construct a real-time intraoperative thrombosis risk prediction model by integrating PINN flow analysis, branch vessel flow conditions, hemodynamic thrombotic indicators, and real-world clinical outcomes. This project provides a new perspective for the assessment of thrombosis-related complications in AAA. As the major product to be expected, the surgical simulation software and algorithms have valuable potential in aiming clinical decision-making and promoting the innovation and transformation of surgical instruments.

Computer Vision-based Modeling for Aging Evaluation and Its Application in Anti-aging

Principal Investigator	Ke Si, PhD
PI Primary Affiliation	Zhejiang University
Co-Investigator(s)	Xiaogang Xu, PhD; Junnan Xu, MS; Hui Yu, PhD; Kaihua Liu, BS

PROJECT DESCRIPTION

At present, population aging has become a global phenomenon. Particularly in our country, the situation is increasingly severe. Aging and its related diseases have imposed a heavy burden on social development and people's lives. Among them, behavioral abnormalities triggered by the decline of brain function are an important manifestation of aging. Therefore, establishing effective aging models and intervention methods is a crucial issue in scientific research. However, the existing molecular and cellular models, as well as single-behavior outcome and subjective aging index assessments, still cannot meet practical needs. For these reasons, this project proposes an innovative computerized visual aging evaluation system. We will study the multi-dimensional behavioral changes in aging animal models of different ages, establish a comprehensive behavioral dataset, and combine it with multi-omics sequencing technology to further optimize system performance. By developing multimodal feature extraction and behavioral analysis techniques, we aim to construct an efficient aging behavioral analysis scheme and apply it to human behavioral aging evaluation and screening of anti-aging drugs.

The core innovation of this project lies in establishing a multi-dimensional computer vision behavioral aging evaluation model based on the joint optimization of genomics, proteomics, transcriptomics, and metabolomics across movement, memory, and emotion. This breaks away from the traditional single-behavior results and provides a more accurate and objective evaluation mechanism. We will establish an intelligent system integrating aging evaluation and anti-aging treatment screening, providing high-throughput and precise research tools for research on the mechanisms of aging-related diseases and the development of anti-aging drugs.

Defining the role and mechanism of adipose tissue transplantation in aging

Principal Investigator	Yu Zhao, PhD
PI Primary Affiliation	Institute of Radiation Medicine, Chinese Academy of Medical Sciences and Peking Union Medical College
Co-Investigator(s)	Yingyi Zhang, PhD; Qianying Lu, PhD

PROJECT DESCRIPTION

Functional changes in adipose tissue are closely linked to the aging process, and the thermogenic properties of brown and beige fat offer a novel perspective for studying metabolic diseases and aging. However, the precise mechanisms and methods for inducing brown and beige fat and activating its anti-aging activity remain unclear. In our previous research, we utilized fat transplantation and ex vivo gene-editing techniques to uncover a new molecular mechanism for the browning of white fat and successfully established a long-lived mouse model, Fbf1tm1a/tm1a. We discovered that the loss of the cilia gating gene FBF1 significantly promotes the browning of

white fat precursor cells, creating a unique "healthy obesity" phenotype. Transplanting these special "healthy obese" fat cells back into mice can improve their metabolic levels and extend their lifespan by 50%. We will further explore the potential of fat transplantation technology in the anti-aging process, optimize the transplantation method to enhance efficiency, and conduct a comprehensive assessment of its long-term effects and safety. The advantages of this project over other anti-aging technologies or products are (1) fat transplantation, as a mature technique in the field of medical aesthetics, has high safety when applied to the field of longevity treatment with low safety risks, (2) ex vivo gene-editing technology of adipocytes eliminates off-target effects of editing plasmids or viruses in the body, and (3) autologous fat transplantation reduces immune rejection reactions, resulting in fewer side effects.

Development and application of a simulation system for transcatheter aortic valve replacement based on virtual simulation and 3D printing

Principal Investigator	Huiping ZHANG
PI Primary Affiliation	Beijing Hospital
Co-Investigator(s)	None

PROJECT DESCRIPTION

Aortic Stenosis (AS) is a common valvular heart disease with a prevalence of 3% to 7% in the population over 65 years of age. In the elderly population, transcatheter aortic valve replacement (TAVR) has gradually become the standard alternative treatment for patients with severe AS who are at high surgical risk or have contraindications to surgical procedures. TAVR technology has become increasingly mature in China, but the aortic valve and perivalvular adjacent structures are complex. Considering the complexity of the aortic valve and perivalvular adjacent structures, the larger individual differences in the structure of the aortic root, and the complexity of the TAVR procedure, there are many uncertainties in the precise implementation of TAVR procedure, the evaluation of the postoperative outcome, and the prediction of perioperative complications.

This project is oriented to the clinical demand for simulation and accurate prediction of TAVR procedure in the elderly, to develop virtual simulation technology based on 3D printing and computational fluid dynamics, and to apply it in TAVR procedure, in order to guide the accurate implementation of TAVR procedure.

Development and Application Research of an Optical High-Resolution Microscopy System for Neurointerventional Endoscopic Imaging Catheters

Principal Investigator	Miaowen Jiang, PhD
PI Primary Affiliation	Beijing Institute of Brain Disorders, Capital Medical University; Xuanwu Hospital, Capital Medical University
Co-Investigator(s)	Chen Zhou, MD&PhD Ming Li, PhD Xunming Ji, MD&PhD

PROJECT DESCRIPTION

Traditional intravascular endoscopes have limited application in neuro-vasculature due to poor visualization through blood and size constraints. The applicant proposes to develop an intravascular optical imaging catheter for neuro-intervention based on optical coherence principles, which will provide high-quality direct visualization images while meeting the miniaturization requirements for navigation in small intracranial vessels. Building upon a preliminary prototype, this project focuses on the optical components at the catheter tip, catheter design, and animal validation, using micro- and nanoscale optical components and an external charge-coupled device (CCD)

camera to generate images, while utilizing an optical fiber to establish the conduit and minimize the diameter of the interventional imaging probe.

Development and Promotion of Endoscopic Hand Suture System for Elderly Patients Undergoing ESD Surgery

Principal Investigator	Lizhou Dou, MD
PI Primary Affiliation	Cancer Hospital, Chinese Academy of Medical Sciences
Co-Investigator(s)	Jiangtao Chu, MD;Hairui Wu, MD;Shun He, MD

PROJECT DESCRIPTION

Screening and early diagnosis and treatment of gastrointestinal malignant tumors are key components of China's strategy to shift the focus of cancer prevention and treatment. Currently, endoscopic submucosal dissection (ESD) has become a significant option for treating early gastrointestinal tumors and precancerous lesions. Although ESD is considered a "super minimally invasive" treatment, studies indicate that it still has a certain rate of adverse events, particularly delayed postoperative bleeding, which can occur in 2.2%-11% of cases. As the nation gradually enters an aging society, the issues of high delayed bleeding probability among elderly patients on long-term anticoagulants have become increasingly serious. There is currently a lack of ideal clinical strategies to address this.

This study aims to develop a novel endoscopic hand suturing technique (EHS) and corresponding surgical instruments and materials, which can be used for the complete closure of larger mucosal defects after ESD, fundamentally addressing delayed bleeding and perforation problems in elderly high-risk patients. Preliminary studies abroad have confirmed the feasibility and safety of using EHS for closing gastric ESD defects; however, there are no multicenter clinical data on using EHS to close gastrointestinal mucosal defects in China. This research will employ the EHS technique to close gastrointestinal wounds post-ESD and will conduct a multicenter study to validate the success rate and lasting closure effects of the EHS technique, assessing its safety and reliability while further developing, improving, and upgrading the endoscopic suturing system.

Development of Long-Lasting Anti-Tumor and Anti-Aging T Cells

Principal Investigator	Guideng Li, PhD
PI Primary Affiliation	Suzhou Institute of Systems Medicine, Chinese Academy of Medical Sciences, Peking Union Medical College
Co-Investigator(s)	Hongcheng Cheng, PhD; Ermei Xie, MS; Yajing Qiu, MS; Jing Du, MS; Yue Xu, MS; Zhe Wang, PhD

PROJECT DESCRIPTION

Adoptive T cell therapy (ACT) holds significant promise for treating tumors and age-related diseases, including autoimmune disorders. The effectiveness and longevity of ACT depend largely on the differentiation state of the transferred T cells. Currently, there is a lack of cost-effective and efficient methods for inducing a low-differentiation state in T cells and achieving prolonged in vitro expansion. The project aims to develop new methods for the large-scale preparation of low-differentiated anti-tumor and anti-aging T cell products, so as to break the technical bottlenecks in the large-scale preparation of long-lasting T cell products and to promote the clinical application of universal, highly efficient, and low-cost T cells.

Our preliminary analysis of single-cell sequencing data identified a notable increase in mannose metabolism in stem-like progenitor exhausted CD8 + T cells. We also found that supplementing the culture medium with mannose promotes the differentiation of these stem-like T cells, enhancing their persistence and anti-tumor activity in vivo. Therefore, the project plans to further study the molecular mechanism of mannose metabolism

regulating the stemness differentiation of T cells, and generate TIL, TCR-T, CAR-T and universal CAR-T cell products targeting tumor and autoimmune diseases through genetic engineering modification and prolonged D-mannose treatment. Additionally, the potential application of mannose in anti-aging and anti-uPAR CAR-T products will be explored.

Development of PGK1 Activator as Innovative Neuroprotective Drug

Principal Investigator	Lei Liu, PhD
PI Primary Affiliation	School of Basic Medicine, Capital Medical University
Co-Investigator(s)	None

PROJECT DESCRIPTION

AnCel-11 represents a significant therapeutic advancement in addressing the decline of brain glucose metabolism, a critical factor in brain aging and a hallmark of neurodegenerative diseases such as Alzheimer's disease (AD). Existing therapies to activate glycolysis are inadequate, with terazosin—a Pkg1 activator—limited by insufficient glycolytic enhancement, alpha1-adrenergic receptor-related side effects, and inhibitory effects on Pkg1 at high doses. These shortcomings restrict its clinical utility.

Drug Screening and Clinical Translation Research on Pathogenic Targets for Testicular Aging and Hypogonadism

Principal Investigator	Zhi Zhou, PhD
PI Primary Affiliation	School of Life Science and Technology, Shanghaitech University
Co-Investigator(s)	Zhiwen Deng, PostDoc; Songzhou Jiang, RN; Xiaoyang Chen, PhD; Houkun Lv, PhD; Jiajun Zheng, PhD; Kunkun Yu, MS; Qianshun Yao, MS; Yueyue Liu, MS

PROJECT DESCRIPTION

The aging population, coupled with increasing concerns regarding testicular aging and hypogonadism, has led to growing prevalence of male infertility and endocrine disorders that significantly affect quality of life. Currently, the only available treatment is testosterone replacement therapy (TRT), which is associated with various side effects, including testicular atrophy, impaired spermatogenesis, and an increased risk of all-cause mortality rate.

To better understand the underlying mechanisms of testicular aging and develop alternative therapeutic strategies, our team previously established a comprehensive single-cell atlas of the human testis across the lifespan. Using both cellular and animal models, preliminary research revealed that abnormal lysosomal acidification in Sertoli cells is a key factor contributing to accelerated testicular aging. Furthermore, targeting lysosomal ion channels with ML-SA1 to restore proper lysosomal acidification demonstrated the ability to repair Sertoli cell function and alleviate the pathological effects of testicular aging. The precise mechanisms driving lysosomal acidification abnormalities during testicular aging remain unclear. Moreover, ML-SA1, despite its promising effects, has limitations related to its poor druggability.

This project aims to further elucidate the mechanisms by which testicular aging disrupts lysosomal acidification and to identify one or two critical therapeutic targets that can be leveraged for treating testicular aging. In addition, the small molecule compounds will be screened to restore lysosomal acidification and mitigate the pathophysiological consequences of testicular aging.

Early diagnosis and risk prediction modeling of coronary heart disease based on multimodal imaging big data

Principal Investigator	Chun Lin Li, PhD
PI Primary Affiliation	Capital Medical University
Co-Investigator(s)	Xu Zhang, PhD; Min Fu Yang, MD; Xian Tao Song, MD; Ying Liang, PhD; Jing Wei, PhD; Li Wei Sun, PhD; Xin Ling Geng, PhD; Xia Li, PhD; Miao He, MS; Zhong Tian Guan, PhD; Yu Bo Liu, MS; Yu Shuang Liu, MD; Bi Xi Chen, PhD

PROJECT DESCRIPTION

Coronary Heart Disease (CHD) is the leading cause of death worldwide, often progressing without symptoms until severe cardiovascular events occur. Early diagnosis is crucial to prevent plaque rupture, thrombosis, and associated complications such as myocardial infarction. This project focuses on CHD early diagnosis using multimodal data by developing key tissue segmentation models to extract coronary artery and epicardial fatty structures and identify novel biomarkers. Building on this, an early diagnostic model for CHD is proposed, incorporating a progressive fusion algorithm to leverage complementary information from multimodal data. The approach captures key heterogeneous features that differentiate CHD patients from healthy individuals, enabling precise diagnosis. Furthermore, a migration paradigm is designed to adapt the diagnostic model to new datasets under unlabelled conditions, addressing challenges in clinical deployment. This paradigm facilitates the practical application of deep learning models in clinical settings. Overall, the project provides an innovative method for predicting structural and functional changes in coronary arteries, contributing to the early diagnosis and management of CHD.

Efficacy and Safety of Intra-arterial Hypothermia with Extracorporeal Circulation Combined with Thrombectomy Therapy in Severe Acute Ischemic Stroke

Principal Investigator	Chuanjie Wu, PhD
PI Primary Affiliation	Xuanwu Hospital Capital Medical University
Co-Investigator(s)	Chuanhui Li, PhD; Chengbei Hou, PhD; Xuehong Chu, MD; Wanwan Zhang, MD; Erlan Yu, MD

PROJECT DESCRIPTION

Despite high revascularization success rates (>80%) in acute ischemic stroke, particularly large vessel occlusion, over half of patients experience poor outcomes. Bridging this gap remains crucial. Intra-arterial targeted temperature management (TTM) offers promising neuroprotection, addressing limitations of previous therapeutic hypothermia studies (systemic side effects, ineffective cooling, and lack of revascularization consideration). Post-revascularization, intra-arterial TTM effectively reduces brain temperature while preserving core body temperature. Our research introduces a novel approach: an autologous blood-based TTM device for safe, precise cooling, combined with a novel porous, flexible catheter incorporating micro-scale hollow nanospheres to enhance heat exchange. Multi-scale simulations will evaluate the catheter's thermal and mechanical properties.

This synergistic approach aims to achieve safe and effective brain-targeted cooling post-revascularization in severe stroke, potentially improving patient outcomes and offering a new treatment strategy.

Endplate Mechanics Matched Interbody Fusion Device In Osteoporotic Patients

Principal Investigator	Qiang Yang, MD, PhD
PI Primary Affiliation	Tianjin Hospital
Co-Investigator(s)	Xinlong Ma, MD; Weijia William Lu, PhD; Chao Chen, MD, PhD; Xun Sun, MD, PhD; Hanming Bian, MD; Yuanzhi Weng, MSc

PROJECT DESCRIPTION

Intervertebral fusion surgery is a common treatment for degenerative spinal diseases, but subsidence of fusion cages post-surgery, with an incidence rate of 15.9% to 70%, can lead to significant complications. Our project addresses this by developing 3D-printed porous titanium alloy cages that match the mechanical properties of the patient's endplate. Using QCT software, we assess the bone density and elastic modulus of the endplate to design cages with corresponding mechanical characteristics. We offer two models: standardized cages with three porosity levels for different bone densities and personalized cages for patients with unique endplate mechanical properties, particularly for elderly with severe osteoporosis. The goal is to improve surgical outcomes, reduce cage subsidence, enhance therapeutic efficacy, and improve patient quality of life, while also reducing the medical burden on society.

Engineered neural stem cells to detect aging-related vascular damage and repair the blood-brain barrier

Principal Investigator	Tianwen LI, PhD, MD
PI Primary Affiliation	Huashan Hospital, Fudan University
Co-Investigator(s)	Jianhong ZHU, PhD, MD Qisheng TANG, PhD Tongming ZHU, PhD, MD Peng WANG, PhD, MD Fengshi LI, PhD, MD Jingyu YU, PhD, MD Xiao FAN, PhD, MD Chen CHENG, PhD, MD

PROJECT DESCRIPTION

As individuals age, the blood-brain barrier (BBB) undergoes structural and functional deterioration, including loosening of endothelial cell junctions, reduced transporter function, increased inflammation, and oxidative stress. BBB disruption allows harmful substances and immune cells from the blood to infiltrate the brain, triggering inflammation and damaging neurons and oligodendrocytes. Moreover, BBB disruption is implicated in various neurodegenerative diseases, such as Alzheimer's (AD) and Parkinson's (PD), where it accelerates the accumulation of harmful proteins like β -amyloid and α -synuclein, exacerbating disease progression. Effective BBB repair could significantly delay aging and provide novel therapeutic strategies for neurodegenerative diseases.

Neural stem cells (NSCs), known for their self-renewal and differentiation potential, mediate neurorepair through immune modulation and local proliferation. However, their direct protective role in BBB repair remains unclear. In this study, we identified CD40 as a key molecule involved in BBB disruption related to aging and AD. Using synthetic biology, we engineered Anti-CD40::SynNotch NSCs, which exhibit a natural tropism for BBB disruption and incorporate a reporter protein strategy to monitor age-related BBB breakdown. Furthermore, we modified the

BBB repair protein Wnt7a (Wnt7a-K190A) for enhanced safety and efficacy. Upon recognition of CD40, engineered NSCs produce and secrete Wnt7a-K190A, activating BBB repair pathways through Gpr124 receptor binding on endothelial cells.

This approach, utilizing SynNotch technology and nasal administration, combines precision, safety, and therapeutic potential for treating AD, PD, and delaying brain aging by stabilizing the BBB and maintaining homeostasis.

EXpress Prevent Rural oldEr adults' falls and fractureS (ExPress)

Principal Investigator	Yao YAO, M.D.
PI Primary Affiliation	Center for Healthy Aging Transdisciplinary Sciences (CHATS), China Center for Health Developments, Peking University
Co-Investigator(s)	Lihai ZHANG, M.D.; Faqin LV, M.D.; Zengguang HOU, PhD; Shibo Cai, PhD; Jing SUN, PhD; Chen WANG, PhD; Shaojie LI, PhD; Yuling JIANG, MSc; Wenjian ZHOU, PhD; Yang HU, MSc; Mingzhi YU, MSc; Yifei WU, MSc; Jing WU, MSc; Zhenhan YU, Ms.

PROJECT DESCRIPTION

ExPress Program closely revolves around the dual national strategies of “actively responding to population aging” and “rural revitalization”. By establishing a “Village doctor + Express/courier” health management model for primary healthcare (village doctor-led risk screening, health education and township courier fall intervention packages delivered to the door), it conducts graded health management of the risks of falls and fractures among rural older people, and therefore improves their functional independence and quality of life.

In situ editing of T cells with biomimetic lipid nanoparticles for the treating of senescence related disorders

Principal Investigator	Lei Miao, PhD
PI Primary Affiliation	State Key Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, Beijing, China. Beijing Key Laboratory of Molecular Pharmaceutics, School of Pharmaceutical Sciences, Peking University, Beijing, China.
Co-Investigator(s)	Mi Deng, PhD; Zhitao Ying, PhD

PROJECT DESCRIPTION

Aging is an inevitable part of the life process that significantly impacts an individual's health and quality of life. The clearance of senescent cells accumulated in the body is an effective anti-aging strategy that is gaining increasing attention. However, existing methods for clearing senescent cells have their limitations: small molecule drugs may have off-target toxicity; cell therapies targeting specific senescence markers such as NKG2D are expensive and can have serious side effects; while mRNA-based in vivo CAR T therapies have the advantages of good targeting, low cost, and safety and controllability, they currently rely on antibody-modified delivery carriers, which may cause side effects such as T cell exhaustion. In response to these challenges, this project is dedicated to developing a biomimetic lipid delivery system that does not depend on antibody modification to efficiently deliver mRNA to T cells, activate the production of anti-aging CAR T cells in the body, and achieve the specific clearance of senescent cells.

Injectable vascular organoid for treating ischemic diseases

Principal Investigator	Kai WANG, PhD
PI Primary Affiliation	Department of Physiology and Pathophysiology, School of Basic Medical Sciences, State Key Laboratory of Vascular Homeostasis and Remodeling, Clinical Stem Cell Research Center, Peking University Third Hospital, Peking University
Co-Investigator(s)	Xi WANG, PhD; Weijing KONG, PhD candidate; Zihang PAN, PhD candidate

PROJECT DESCRIPTION

Ischemic diseases, caused by blood vessel occlusion or disrupted hemodynamics, result in tissue ischemia, hypoxia, and cell death. These conditions are a leading global cause of mortality, significantly affecting health, life expectancy, and healthcare systems. While coronary intervention and bypass surgeries offer treatment for ischemic heart disease, critical lower limb ischemia, especially diabetic foot ulcers, lacks effective therapies, necessitating advanced research. Recent advancements highlight the therapeutic potential of stem cell-derived endothelial cells, mesenchymal stem cells, and organoids. Organoids, as 3D multicellular assemblies, mimic organ structures and functions, offering promising avenues for disease modeling and regenerative treatments. Vascular organoids, in particular, show potential for ischemic disease treatment, though challenges like differentiation efficiency, immune rejection, and engraftment remain.

Our research focuses on refining differentiation protocols for vascular organoids to enhance angiogenesis and clinical applicability. Leveraging transcription factors ETV2 and NKX3.1, we have developed efficient methods to differentiate pluripotent stem cells into vascular endothelial and smooth muscle cells. Using small molecules and growth factors in a 3D bioreactor, we have successfully created vascular organoids capable of forming perfusable networks in vitro and in vivo. This project aims to optimize these organoids and apply them to treat acute myocardial ischemia and critical lower limb ischemia, paving the way for clinical translation and innovative ischemic disease therapies.

Innovative drug research and development of Z583 for the treatment of autoimmune disease

Principal Investigator	Tiantai ZHANG, PhD
PI Primary Affiliation	Institute of Materia Medica, Chinese Academy of Medical Sciences
Co-Investigator(s)	Lan SUN, MD; Chengjuan CHEN, PhD; Gaona SHI, PhD; Yu ZHOU, PhD; Yazi WEI PhD

PROJECT DESCRIPTION

Autoimmune diseases are a large category of diseases that cause tissue damage due to immune tolerance disorders of the body. Non-receptor tyrosine kinase (JAK) is a new target for the treatment of autoimmune diseases, which has been recognized after epoxidase in the last 40 years, and contains 4 subtypes. Due to non-selective inhibition, JAK inhibitors currently on the market have clinically critical problems such as serious opportunistic infections, anemia and other cardiovascular events, and many instructions of non-selective JAK inhibitors have been required by FDA to have a black box warning. Therefore, the R&D of selective JAK inhibitors reflects the necessity in terms of the severity and urgency of the disease, the shortage of therapeutic drugs, the novelty of the target, and overcoming the side effects of current non-selective JAK inhibitors. In the previous stage, we obtained a new selective JAK3 small molecule inhibitor of Z583 (Patent No. ZL201811078582.X in China and US11993603B2 in USA). The IC₅₀ of Z583 was 0.10 nM, which was > 4500 times of the selectivity for JAK1, JAK2 and Tyk2 subtypes. Z583 showed a clear anti-RA effect on CIA model with the dose of 3mg/kg (p.o.). The toxicity evaluation showed no cardiotoxicity or mutagenicity, especially the acute toxicity test in rats given large doses for four consecutive weeks showed no routine blood and abnormal

liver and kidney function, thus avoiding the occurrence of cardiovascular events such as anemia. Z583 is a highly selective JAK3 inhibitor with great potential for the treatment of autoimmune diseases.

Innovative medical device research and development for precise management of airways within lung segments and exposure of anatomical boundaries of lung segments

Principal Investigator	Chao Ding, MD
PI Primary Affiliation	Cancer Hospital, Chinese Academy of Medical Sciences Peking Union Medical College
Co-Investigator(s)	Xue QI, MD

PROJECT DESCRIPTION

This study aims to develop original medical devices "pulmonary segmental bronchial tubes",a prospective randomized controlled applied basic research will be conducted for clinical subjects undergoing thoracoscopic pulmonary segmental anatomical resection surgery. After achieving single lung ventilation with collapsed lung on the affected side, the pulmonary segmental bronchial tube will be delivered to the target pulmonary segmental bronchial opening through the bronchoscopy operation channel. The target pulmonary segment will be selectively expanded by inflating the pulmonary segmental bronchial tube, accurately revealing the "target pulmonary segment anatomical boundary map", helping thoracic surgeons quickly and accurately identify the anatomical range of the target pulmonary segment during surgery, verify its clinical safety and effectiveness.

Intelligent epilepsy diagnostic monitor

Principal Investigator	Xu ZHANG, PhD
PI Primary Affiliation	School of Biomedical Engineering, Capital Medical University
Co-Investigator(s)	Jinglong WU, PhD; Penghu WEI, PhD; Mingqiang HUANG, PhD; Yanfeng YANG, PhD; Yutang LI, BE; Hui OUYANG, BE; Xiaoyue LOU, BE; Jihan WANG, BE; Jie HAN, BE

PROJECT DESCRIPTION

Epilepsy is the third most common neurological disorder in the elderly, and its diagnosis is often complicated by coexisting diseases. To enable accurate diagnosis and seizure detection for elderly patients, our project aims to develop an intelligent epilepsy monitoring device. This device integrates advanced algorithms for epilepsy diagnosis, seizure detection, and prediction designed. Then these algorithms will be implemented on a FPGA chip, enabling efficient, low-power, wireless real-time EEG acquisition and monitoring. This innovative approach aims to simplify the diagnostic process and improve the management of epilepsy in elderly patients, enhancing their quality of life and safety.

Intelligent rehabilitation system of hand function based on brain-computer interface

Principal Investigator	Xiaogang Chen, PhD
------------------------	--------------------

PI Primary Affiliation	Institute of Biomedical Engineering, Chinese Academy of Medical Sciences and Peking Union Medical College
Co-Investigator(s)	Hongyan Cui, PhD; Zexin Pang, MD; Yiming Shao, MD; Ruqing Zhang, MD

PROJECT DESCRIPTION

Stroke has become the leading cause of death and disability among adults in my country. The difficulty in reconstructing fine motor skills of the hand has become an international problem in the field of stroke motor function rehabilitation, which has caused a serious burden on families and society. About 20% to 30% of stroke patients are unable to undergo compulsory exercise therapy or other rehabilitation methods due to severe limb motor dysfunction on the affected side. The closed-loop motor rehabilitation training system based on brain-computer interface (BCI) provides a new way to improve the level of motor rehabilitation and is one of the important development directions in the field of neurorehabilitation in the future.

This project aims to develop an intelligent rehabilitation system for hand function based on BCI, carry out technical application verification for neurorehabilitation scenarios, realize a highly comfortable and fast-response neurorehabilitation system, improve the reorganization or compensation of the patient's brain nerve conduction function, promote the recovery of motor function and somatic sensory function, and improve the level of motor function rehabilitation. recovery of motor function and somatic sensory function, and improve the level of motor function rehabilitation.

Medical & Social Work Collaboration: Building a medium to long-term integrated Care Referral System for Senior Patients

Principal Investigator	Li WEI, MSSC
PI Primary Affiliation	Peking Union Medical College Hospital
Co-Investigator(s)	Chunhou LI, MPH; Lin KANG, MD; Xuan QU, MD; Xin QIAN, MA&MSW

PROJECT DESCRIPTION

With the growth of aging population in China, the demand for integrated medium and long-term healthcare management for senior patients is increasing, and the requirements for individualized patient care plan is also increasing. Currently, our country is actively building a senior care service system that adapts to an aging society with unprecedented determination and strengths through multi-dimensional measures such as policy guidance, service innovation and social participation, and strives to enable every senior person to enjoy a happy, healthy and dignified aging life. The Social Work Department and the Geriatric Medicine Department in Peking Union Medical College Hospital jointly planned a medium to long-term integrated care referral system for senior patients. It aims to develop care plan and integrate the medium and long-term healthcare services for senior patients when discharging from hospital through a scientific and technological system. The system will integrate clinical medical data and social service resources, and provide individualized health care plans for senior patients upon discharge. This innovation not only improves the accuracy and timeliness of support services. It can also track services, and provide alternative community care options for discharged patients, thereby improving their quality of life. Through the mutual collaboration of medical professionals and medical social workers, the average length of stay and bed occupancy rate can be reduced, and medical efficiency can be improved. The implementation of this system can be a model to other medical institutions, and promote the overall progress of medium to long-term integrated care management services for seniors.

Multitarget mechanism and application of small molecule compound PL402 in the treatment of Alzheimer's disease

Principal Investigator	Yujun Hou, PhD
-------------------------------	----------------

PI Primary Affiliation	Tongji University
Co-Investigator(s)	Jianhuang Xue, PhD

PROJECT DESCRIPTION

Alzheimer's disease (AD), characterized by progressive neurodegeneration, cognitive and memory impairments, and neuronal loss, is a major global health concern in the aging population. Current treatments have limited efficacy in halting AD progression. This project focuses on PL402, a novel compound derived from natural products. Initial tests have demonstrated its potential to improve cognitive function in AD patients. In this project, we will comprehensively evaluate PL402's effects on AD model mice, including spatial learning and memory, social behavior, locomotor functions, and muscle strength. Moreover, the impacts of PL402 on AD pathologies such as A β plaque, neuroinflammation, cellular senescence, and its role in neuronal survival and neurogenesis will be investigated. Mechanistically, the influence of PL402 on gene expression and immune signaling will be analyzed. Previous results showed that PL402 could suppress the cGAS-STING pathway. We aim to clarify how PL402 modulates this pathway to reduce neuroinflammation and achieve therapeutic outcomes. Epigenetic changes in the PL402-treated AD mice have also been observed. Future work will focus on deciphering how these epigenetic changes affect gene expression and AD progression, and exploring whether PL402 can alleviate neuroinflammation by regulating epigenetic modifications, potentially providing a new treatment basis. To ensure clinical applicability, we will conduct pharmacodynamics and toxicological studies to assess the safety and efficacy of PL402 and determine its tissue distribution and toxicity at different doses. The project is expected to provide a potential option for AD treatment and new insights into relevant mechanisms, contributing to an improved prognosis for AD patients.

NIEGP: Pioneering Geriatric Depression Risk Stratification with a NeuroImaging ExposoGenomics intelligent Platform

Principal Investigator	Jiayuan XU, MD
PI Primary Affiliation	Tianjin Medical University General Hospital
Co-Investigator(s)	Nana Liu, MD; Qiaojun Li, PhD; Guoshu Zhao, MD candidate; Nannan Zhang, MS candidate; Shaoying Wang, MS candidate

PROJECT DESCRIPTION

Geriatric depression is a common mental disorder that significantly diminishes the life quality for the aging global population. Accurately predicting those at risk is crucial, yet we confront significant challenges due to the scarcity of reliable biomarkers.

In this project, our team introduces the innovative NeuroImaging ExposoGenomics (NIEG) strategy, designed to uncover the neural mechanisms by which genetic and environmental factors influence cognition and mental health. By harnessing genetic statistics, remote-sensing, and neuroimaging technology, we aim to identify neuroimaging biomarkers based on NIEG and to develop risk prediction and stratification tools for depression leveraging machine learning.

Our team has developed a NIEGP platform, which offers personalized NIEG depression risk scores, risk genes, lifetime risk environment exposures, neuroimaging biomarkers, and predictive tools to address the unmet needs in mental disorders, including depression. Our groundbreaking findings reveal that participants with higher CRHR1 genetic risk, living in urban environments characterized by poverty, reduced greenness, and complex street networks, especially during adolescence, exhibit reduced reward-processing brain volumes and severe affective symptoms. The risk of these individuals developing depression has increased fivefold (Nat Med, 2023; Nat Hum Behav, 2022). The NIEGP application provides personalized guidance to individuals with risk genes, targeting the risk time window under specific environmental exposures, to alleviate depressive symptoms and prevent the onset of depression. Our interdisciplinary team is based at the Tianjin Key Lab of Functional Imaging (FUNI) in China.

Our lab's flagship program, CHIMGEN, initiated in 2015, targets the neural mechanisms underlying mental disorders that affect over one billion people worldwide. Over the past decade, we have collected comprehensive genetic, environmental, neuroimaging, and behavioral data from 13,000 Chinese-Han individuals across 31 leading centers in China, creating the world's first NIEG dataset for a non-Caucasian population. By integrating with other international datasets, CHIMGEN offers a unique opportunity to explore the cross-ancestry effects of genomics and environment on global mental health disorders.

Novel 3D Bioprinting Pan-cancer Platform for Personalized Medicine and Mechanism Research

Principal Investigator	Yu Wang, MD
PI Primary Affiliation	Peking Union Medical College Hospital
Co-Investigator(s)	Huayu Yang, PhD; Yilei Mao, MD; Wenbin Ma, MD; Jiangang Zhang, MD; Huiyu Yang, MD; Ying Shan, MD; Ying Jin, MD; Jiaming Wu, MD; Hao Xing, MD; Yuekun Wang, MD

PROJECT DESCRIPTION

Malignant tumors have become the leading cause of death in China. The incidence of cancer in China has followed an increasing trend due to population aging. Currently, the systematic treatment of malignant tumors still greatly relies on the empirical choices of physicians. With the significant interpatient heterogeneity of tumors, determining the appropriate treatment plan for each individual remains a major challenge in the field of cancer systemic therapy. Our team propose using 3D bioprinting to construct patient tumor-derived avatars (PTA) with semi-automated drug sensitivity testing to achieve personalized medication. Compared to competitors on the market, 3D bioprinted tumor models are currently the only in vitro modeling technology that can provide drug sensitivity results before clinical medication. This technology offers advantages such as short turnaround time, high modeling success rate, good fidelity, and low cost. Since the research team first constructed the world's first primary hepatocellular carcinoma 3D bioprinted model in 2020, we have now successfully established 3D-PTA in more than 10 cancer types, with success rate of more than 95% in model construction and standardized procedures for drug sensitivity testing. This project is expected to reduce ineffective medical expenditures and ultimately rewrite medical guidelines, achieving both social impact and health economic benefits, thereby propelling China's precision oncology practice into a new era.

Novel Strategy and Equipment Development for Non-Invasive Treatment of Hydrocephalus--taVNS

Principal Investigator	Xiuyun LIU, PhD
PI Primary Affiliation	Tianjin University
Co-Investigator(s)	Dong MING, PhD Kuo ZHANG, PhD Meijun PANG, PhD Runnan HE, PhD Xiqi JIAN, PhD Huijie YU, PhD Xizi SONG, PhD Jinrui DONG, PhD

PROJECT DESCRIPTION

Hydrocephalus, a prevalent condition among the elderly population, exerting a significant influence on their health and longevity, which lacks noninvasive treatment. The predominant therapeutic approach involves

neurosurgical interventions, such as the insertion of cerebrospinal fluid shunts, which has a high risk of complications, imposing a considerable financial burden on the affected patients. Thus, we are in great need to develop novel strategies and devices for the treatment of hydrocephalus, aiming to facilitate safe, efficient and cost-effective treatment. Transcutaneous vagus nerve stimulation (taVNS), a non-invasive neuromodulation technique, has garnered substantial interest in recent years, largely due to neuroscientific advancements, and has been recognized as a potentially effective therapeutic intervention for epilepsy, stroke, and other brain disease. The preliminary research carried out by the project team has uncovered, for the first time, taVNS can significantly enhance the behavioral, pathological, and imaging outcomes in hydrocephalus patients. Based on these findings, the project plan to conduct detailed animal experiment, clinical trial assessments, mechanistic inquiries, and develop innovative taVNS device for hydrocephalus treatment. We aim to afford hydrocephalus patients with a safer and convenient thereby, and improving the quality of life for elderly patients.

Study of novel anti-aging strategies targeting aged neutrophils

Principal Investigator	Minghong Jiang, PhD
PI Primary Affiliation	Department of Immunology, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences
Co-Investigator(s)	Junmin Wang, PhD; Yuyang Wang, PhD; Leilei Ren, MS

PROJECT DESCRIPTION

Redox imbalance of immune cells and ROS-driven activation lead to chronic inflammation in ageing organisms, but the mechanism of inflammatory senescence remains a mystery. Neutrophils are important ROS producers. It has been shown that ROS and inflammatory molecules can induce immunosenescence in ageing neutrophils, which have enhanced pro-inflammatory capabilities. They express and secrete a variety of molecules and the high levels of ROS promote chronic inflammation by oxidising biomacromolecules. We hypothesises that excessive oxidative stress in ageing leads to neutrophil immunosenescence and subsequent chronic inflammation. Using healthy elderly and aged mice, we will investigate a novel neutrophil subpopulation that promotes chronic inflammation. Using multiple techniques, we will analyse cell surface receptors, key pathways/genes, proteases, inflammatory factors and pathological death to define the key links between free radicals, inflammation and senescence. We will also map molecular networks and kinetic shifts, investigate whether inhibition of pathways can delay ageing, reveal the novel mechanism, provide a target for new drugs and a basis for identifying specific markers.

Study on self-healing technique of arteriovenous fistula with artificial blood vessel

Principal Investigator	Pingsheng Huang, PhD
PI Primary Affiliation	Institute of Biomedical Engineering, Chinese Academy of Medical Sciences & Peking Union Medical College
Co-Investigator(s)	Yunpeng Bai, PhD; Chuangnian Zhang, PhD

PROJECT DESCRIPTION

Hemodialysis is an important way to maintain life in patients with end-stage renal disease, which relies on long-term reliable vascular access. At present, artificial blood vessels have become an important "lifeline" for hemodialysis patients. However, the blood clotting inflammatory cascade on the inner wall of the artificial blood vessel leads to thrombus and blockage, the immune rejection reaction on the tube body aggravates inflammation and infection, and the mismatch of mechanical properties leads to anastomotic hyperplasia and stenosis. In particular, repeated puncture can easily lead to artificial blood vessel damage and puncture needle bleeding, causing thrombosis, hematoma and false aneurysm, etc., which puts forward higher requirements for the self-

healing performance of artificial blood vessels. Therefore, long-term patency and stability of arteriovenous fistula of artificial vessels are urgently needed to meet the difficulties of hemodialysis treatment. Based on the relationship between the molecular design of artificial vascular materials, structural design and functions of blood vessel, we propose the design concept for engineering artificial blood vessels inspired by the three layers structure of natural blood vessels, using self-healing polyurethane elastomer and zwitterionic hydrogel as the basic materials. It is expected that the bio-mimic self-healing artificial blood vessels could demonstrate similar structure and performance with natural blood vessel, through the reasonable distribution and coordination of the function of artificial blood vessel materials.