

HEALTHY LONGEVITY GLOBAL COMPETITION

2022 Catalyst Awardees

Sponsor: Chinese Academy of Medical Sciences

A minimally invasive trans-choroidal subretinal cannulation system based on a novel resistance sensing mechanical principle of injection

Principal Investigator	Chan Zhao, MD
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Co-Investigator(s)	Youxin Chen, MD; Chaoran Xia, PhD; Chuan Li, PhD;

PROJECT DESCRIPTION

Sub-retinal injection is preferred over intravitreal injection for administration of retinal gene- and cell therapy in patients with retinal degenerative diseases (RDD), such as non-neovascular age-related macular degeneration, retinitis pigmentosa and Leber's congenital amaurosis. There are two approaches for sub-retinal drug delivery, one involves pars plana vitrectomy followed by injection of the agent through a cannula (the trans-vitreous approach) and the other access the sub-retinal space through the sclera and the choroid (the trans-choroidal approach). While the trans-pars plana approach is currently the most commonly used, this approach relies on expensive vitrectomy equipments and requires a high level of surgical expertise; it may also induce complications associated with vitrectomy, such as retinal detachment, cataract, etc. The trans-choroidal approach is less invasive and requires no advanced micro-surgical equipment, and is recently adopted by some pharmaceutical companies addressing sub-retinal delivery of gene therapies. These systems, however, requires a sclerotomy performed on the target eye and suture of the scleral incision after drug delivery. Our group have invented, designed, prototyped, and tested in vivo a novel resistance-sensing mechanical suprachoroidal space (SCS) injector. We are currently developing a minimally invasive trans-choroidal subretinal cannulation system based on the SCS injector, which requires no sclerotomy and suture, and would be far less-invasive than the current approaches. Our novel resistance sensing mechanical principle of injection has a wide range of applications including epidural anaesthesia, trans-parietal-pleura intercostal nerve block during thoracic surgery, etc.

A new strategy for trastuzumab resistance reversal in breast cancer: Construction and application of a multifunctional nanomotor system combining RNAi therapy, starvation therapy, and microenvironmental oxygen supply therapy

Principal Investigator	Xiangyi Kong, MD. & PhD.
PI Primary Affiliation	National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College
Co-Investigator(s)	Jing Wang, MD. & PhD. Yi Fang, MD. & PhD. Zhongzhao Wang, MD. & PhD. Xiangyu Wang, MD. & PhD. Wenxiang Zhang, MD. & PhD.

PROJECT DESCRIPTION

Trastuzumab is an effective drug for the treatment of HER2-positive breast cancer, but the problem of drug resistance severely limits its clinical application. The applicant's previous study found that lncRNA HOTTIP may mediate trastuzumab resistance by activating the Wnt signaling pathway and HOTTIP could be used as a new potential target to reverse this resistance. The present project intends to further explore the molecular mechanisms by which HOTTIP affects the Wnt pathway and thus mediates drug resistance at the cellular and animal levels from perspectives including RNA-binding proteins; on this basis, we will design and synthesize a nanomotor drug delivery system, PFC(si-HOTTIP/GOD)@MnO₂, with multiple functions including delivering specific siRNA to inhibit HOTTIP, promoting tumor glucose deprivation/exhaustion, improving the hypoxic microenvironment, controllable actuation triggered by in vitro ultrasound, and real-time in situ drug release monitoring visualization. We will combine RNAi therapy, tumor starvation therapy, and microenvironmental oxygen therapy to provide a new treatment strategy for reversing trastuzumab resistance. We will investigate the nano-drug's physical and chemical properties, pharmacological effects, anti-drug-resistance effects and mechanisms, and safety. This project is an in-depth expansion of the applicant's preliminary research results supported by previous research funding, and has a good prospect of clinical transformation.

A novel plaque stability prediction model research based on the radiomics and single-cell transcriptomics of pericarotid artery adipose tissue

Principal Investigator	Liu Bao, MD
PI Primary Affiliation	Peking Union Medical College Hospital, Chinese Academy of Medical Sciences
Co-Investigator(s)	Shao Jiang, MS; Lai Zhichao, MD; Li Kang, MD; Xu Leyin, MD; Chen Junye; Du Fenghe; Wang Jiaxian; Zhu Zhan; Shu Keqiang

PROJECT DESCRIPTION

Carotid artery stenosis is an important cause of stroke. Unstable carotid plaque shedding is the main cause of stroke, which has a significant impact on the average life expectancy of the population. Therefore, there is an urgent need for early diagnosis of plaque stability. A large number of recent studies published in Lancet and other journals have confirmed that perivascular adipose tissue (PVAT) is an important factor leading to the aggravation of atherosclerosis. Our group and international studies have confirmed that PVAT inflammation occurs earlier than vascular endothelium. However, at present, the interaction mechanism between PVAT and plaque stability is still unclear, and there is a lack of effective means to determine the stability of carotid plaque before operation. We have carried out plaque stability prediction research based on plaque CT radiomics and plaque 68Ga-FAPI PET/MRI. We have developed the preparation technology of PVAT single cell suspension which could meet the requirements of single cell RNA sequencing and formulated the original carotid artery PVAT image segmentation scheme for radiomics. In this study, we will further establish a cohort of patients with carotid artery stenosis to integrate the pathological section staining results of carotid plaque, PVAT radiomics and PVAT single cell RNA sequencing, which could determine the corresponding relationship between PVAT imaging characteristics and PVAT cellular components and differentially expressed genes. We will construct a novel prediction model of plaque stability based on PVAT imaging features through machine learning and to push the diagnostic boundary of carotid atherosclerotic disease forward.

Active surveillance and precision intervention strategies for elderly patients with non-small cell lung cancer after surgery: predicting patient outcomes and beneficial population from postoperative radiotherapy based on minimal residual disease

Principal Investigator	Zhouguang Hui, MD
PI Primary Affiliation	National Cancer Center/National Clinical Research Center for Cancer/Cancer

	Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College
Co-Investigator(s)	Other Members: Shugeng Gao, MD; Yuchen Jiao, PhD; Kuo Men, PhD; Jianming Ying, MD; Yu Men, MD; Xu Yang, MD.

PROJECT DESCRIPTION

BACKGROUND and AIMS: The populations who can benefit from postoperative radiotherapy (PORT) for non-small cell lung cancer (NSCLC) is unknown. This study aims at predicting the efficacy of PORT and prognosis for elderly patients with N2-NSCLC based on minimal residual disease (MRD) and artificial intelligence (AI).

Study Design: This is an ambispective cohort study based on databases and biobanks of the phase III randomized controlled study and the real-world study. MRD combined with AI will be utilized to build and validate the predictive and prognostic models.

Expected Outcomes: ① Establishing an efficient MRD detection methodology; ② building and validating the predictive and prognostic models; ③ communicating in 1-2 academic conferences; ④ Training one postgraduate.

Fundamentals: ① The applicant is a National Talent Program winner, and has conducted long-term, extensive and in-depth explorations on the issue of PORT in N2 NSCLC. The series of studies represented by the prospective phase III clinical trial PORT-C are of international leading level; ② The backbones of the project have conducted extensive and in-depth research in tumor molecular biology, artificial intelligence and tumor pathology, undertaken a number of relevant national projects, and been selected into a number of national talent programs; ③ The research group has established databases and biobanks from thousands of N2-NSCLC, which meets the research needs; ④ The National Cancer Center is a cancer center integrating medicine, teaching, research, learning and prevention of cancer. There are more than 200 cases of N2-NSCLC receiving radical resection per year.

Application of target intracoronary mild hypothermia treatment system in the treatment of acute myocardial infarction

Principal Investigator	Zhiqiang Pei, MD
PI Primary Affiliation	Taiyuan Central Hospital
Co-Investigator(s)	None

PROJECT DESCRIPTION

Development of therapeutic systems in the cardiovascular field

Application value of electromagnetic navigation and CT guidance in thermal ablation of lung cancer: A prospective cohort study

Principal Investigator	Liang Zhao, M.M.
PI Primary Affiliation	Cancer Hospital Chinese Academy of Medical Sciences
Co-Investigator(s)	Ruochuan Zang, M.D.; Hongliang Wu, M.D.; Wei Tang, M.M.; Lei Zhang, M.D.; Xiawu Zhang, M.D.; Xin Sun, M.M.; Fanmao Meng, M.B.

PROJECT DESCRIPTION

Lung cancer is a malignant tumor with the highest morbidity and mortality in China as well as the world. Although surgical resection is currently recognized as a radical cure for lung cancer, many patients with lung cancer have been found in the middle and late stage, or lost the opportunity for surgery due to other basic diseases, especially for elderly patients. Thermal ablation of tumor has become a good news for patients with tumor, the clinical development is rapid.

Biomechanics and product development of a new spinal total cortical bone thread reducing screw for lumbar endoscopic fusion in elderly patients with osteoporosis

Principal Investigator	Paerhati Rexiti, PhD
PI Primary Affiliation	Xinjiang Medical University
Co-Investigator(s)	Weibin Sheng, PhD; Leilei Xu, MS; Shuiquan Wang, BM; Alafate Kahaer, MS; Dongshan Liu, MS; Xieraili Maimaiti, MS; Abulikemu Maimaiti, MS; Wenjie Shi, BM; Muzaipaer maitusong, BM

PROJECT DESCRIPTION

Cortical bone trajectory (CBT), proposed by Santoni BG in 2009, increase the fixation strength without increasing the hospitalization cost and has become an ideal fixation method for the initial and revision of osteoporosis patients. We found that the traditional CBT technique needs to be further improved. Thus we proposed a modified cortical trajectory (MCBT) technique.

The traditional screw currently used in clinical practice cannot match our modified screw path, which may affect the biomechanical properties of the fixation to a certain extent. With the increasing demand of the elderly for the quality of life as traction, to solve the problem of postoperative failure of fixation in elderly patients with lumbar spinal stenosis and osteoporosis, we designed the combination of a new spinal total cortical bone thread reducing screw and 3D-navigation-template and endoscopy. Based on further realizing minimally invasive and accelerating the rehabilitation of elderly patients, the research results are put into practical application to solve clinical problems.

Through the combination of medicine and engineering, the biomechanical finite element model of lumbar osteoporosis was used to carry out mechanical experiments. The stress distribution between vertebral body and screw under different screws, different techniques, or their combinations under different loads was analyzed, and the factors affecting the stability of screw-bone interface and fatigue resistance were discussed. With the aid of a 3D navigation template and spinal endoscopy, the improvement of lumbar fusion surgery in lumbar spinal stenosis was tried to lay a foundation for its clinical application in patients with osteoporosis.

Cascade targeted multifunctional artificial molecular chaperone for synergistic treatment of Alzheimer's disease

Principal Investigator	Fan Huang, PhD
PI Primary Affiliation	Institute of Radiation Medicine, Chinese Academy of Medical Sciences
Co-Investigator(s)	Jianfeng Liu, PhD; Jinjian Liu, PhD; Chunhua Ren, PhD; Yumin Zhang, PhD; Linzhu Su, PhD

PROJECT DESCRIPTION

Alzheimer's disease (AD) is one of the most serious diseases that threaten human health in the 21st century. Because the pathogenesis of AD is extremely complex which was involved multiple factors including β -amyloid ($A\beta$) aggregation, imbalance of metal ion homeostasis and excessive oxidative brain injury, it is difficult for single-target drugs to meet the treatment needs of AD. Moreover, the current AD drugs still have shortcomings

such as low blood-brain barrier penetration efficiency and poor targeting of AD lesions. Therefore, the project intends to develop a novel cascade targeted multifunctional artificial molecular chaperone through macromolecular self-assembly technology for the synergistic treatment of AD. This artificial molecular chaperone is composed of four parts, micelles with unique hydrophobic micro-domains on the surface which simulating natural molecular chaperones, bioactive small molecule drug in the core of micelles, blood brain barrier targeting peptide and AD lesion tissue targeting peptide modified on the outer layer of micelles. Through the mediation of dual-targeting peptides, this strategy can efficiently cross the blood-brain barrier and then selectively concentrate in the site of AD lesions, achieving the effect of "cascade targeting". At the same time, by simulating the hydrophobic domain of natural molecular chaperones, the surface hydrophobic micro-domains of micelles can effectively inhibit the aggregation of A β , and the combined small-molecule drugs can regulate metal ion homeostasis and reduce oxidative damage, thereby achieving the purpose of "multi-target therapy". This project will open up new avenues for targeted and synergistic treatment of AD.

Development and application of AI-assisted home skeletal muscle health exercise system for the elderly

Principal Investigator	Wang Zhong , M.M.
PI Primary Affiliation	Beijing Tsinghua Changgung Hospital
Co-Investigator(s)	Wang Jingyi , M.M.

PROJECT DESCRIPTION

Aging is a normal physiological process in which body functions inevitably decline with age, especially in skeletal muscle. More and more studies have shown that skeletal muscle health is closely related to health in old age. If we can effectively store skeletal muscle mass and improve the health status of skeletal muscle through behavioral intervention at the early stage, it will be possible to delay aging, realize the change of mode and concept from "supporting for old" to "preventing old", and improve the healthy life expectancy. The research and application of AI assisted skeletal muscle healthy exercise system is of great significance to help the elderly to realize active pension, health and longevity.

Development and application of an intelligent evaluation system for physical function of the elderly supported by multidimensional sensors

Principal Investigator	Sun Chao, MM(Master of Management)
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Co-Investigator(s)	Li Jing MMed, Hu Huixiu MS, Feng Fang MM(Master of Management), Zhangjie MS

PROJECT DESCRIPTION

The number of older people with disability in China is large and still growing fast, with a heavy social burden. We should take earlier interventions to delay the progress of disability. It is important to enhance or maintain the physical function of the elderly to prevent or delay disability because that the decline in physical function precedes disability. However, there is no targeted intervention. The characteristics of physical function changes can provide a target for the exploration of accurate and effective early interventions. At present, the clinical evaluation of physical function mainly depends on the manual evaluation of medical staff. The objectivity and accuracy of the evaluation are lack and a single measurement takes too long as well as consumes a lot of manpower. Above on, this program intends to collect data on the motion trajectory and body composition of the elderly through multi-source sensing technology, and develop an intelligent assessment system for physical function, so as to explore the characteristics of changes in the physical function of the elderly as well as

correlation between physical dysfunction and disability. The study can eventually provide clinical decision-making basis for early identification and precise intervention for older people with disability.

Development and clinical application of ultrasonic electromagnetic navigation system for accurate guidance of targeted transperineal prostate biopsy

Principal Investigator	Wang Jianlong, PhD
PI Primary Affiliation	Chinese Academy of Medical Sciences
Co-Investigator(s)	Liu ming, PhD; Chen Min, PhD; Li Chunmei, PhD; Zhu Hui, PhD; Zhang wei, PhD; Wang Xuan, PhD; Hou Huimin, PhD; Hu Meng, Meng; Guo Dong, Meng; Wang Miao, PhD; Xia Haoran, PhD; Wang Miaomiao, PhD; Lv Zhengtong, PhD

PROJECT DESCRIPTION

Prostate biopsy is the gold standard for preoperative diagnosis of prostate cancer. The magnetic navigation system is a system equipped with electromagnetic vibration tracking technology, which can solve the problem of displaying the puncture needle path during biopsy, thereby assisting the operator to safely and smoothly place the biopsy needle into the target position. At present, the magnetic navigation system has been widely used in biopsy operations of different organs in multiple systems, such as: nerve block in anesthesiology, thyroid biopsy, kidney biopsy, etc. It has been confirmed to improve the success rate of biopsy respectively, and has good application value. However, the biopsy routes tracked and simulated by the existing magnetic navigation system are set in the ultrasound plane, while in prostate biopsy, the insertion direction of the needle is perpendicular to the direction of ultrasonic emission, so the existing technology can not be directly applied to prostate biopsy.

This study intends to optimize the existing equipment, develop a new electromagnetic navigation system for transperineal prostate targeted biopsy, realize real-time navigation of prostate biopsy needle in the model, and record and analyze data and images. Adjust the equipment according to the deviation, develop and upgrade the software to focus on the application of benign and malignant prostate lesions. And, in the completion of model and surgical specimen experiments, the new electromagnetic navigation system was further applied to the clinic, through prospective, single-center, randomized controlled studies, to verify its maneuverability, safety and effectiveness in guiding transperineal prostate targeted biopsy.

Development and Industrialization of Portable Magnetoencephalography Equipment

Principal Investigator	Lu Meng, PhD
PI Primary Affiliation	College of Information Science and Engineering
Co-Investigator(s)	Xiaotong Yang, MD; Ya Ma, BD

PROJECT DESCRIPTION

We investigate a new generation of magnetoencephalography system. The hardware develops a sensor that uses the magnetic effect of atomic spins to realize a technique for measuring weak magnetic fields. The Spin Exchange Retardation Free (SERF) atomic magnetometer is a new type of light-pumped atomic magnetometer that has gained rapid development in recent years. By eliminating the atomic system tracking retardation due to spin exchange collisions, the SERF magnetometer is two orders of magnitude more sensitive than conventional light-pumped magnetometers under the same physical conditions. In addition, the SERF magnetometer is equipped with an adapted analysis software (i.e., MEG Processor) for use not only with the new pMEG but also with existing MEG magnetoencephalography, complete big data processing and analysis, fusion with conventional images such as CT/MIR, complete documentation and accurate localization, and Magnetic Source Locator (MSL), a tool necessary for advanced brain function studies. Source Locator (MSL), a technical software package for imaging functional brain activity; BrainX for brain science, brain behavior, neurological function,

magnetoencephalography (MEG), electroencephalography (EEG), functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation (TMS), etc.

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Development And Promotion of Portable Oral Cancer Screening and Intelligent Diagnosis System Based on Raman Spectroscopy

Principal Investigator	Zhang Tao, DDS, MD, Ph.D
PI Primary Affiliation	Beijing Union Medical College Hospital
Co-Investigator(s)	Guo Chunlan, DDS, MD, Ph.D; Zhu Zhihui, DDS, MD; Li Xing, DDS, B.Ec; Zhao Ruiqi, DDS

PROJECT DESCRIPTION

This project combined Raman spectroscopy analysis technology and artificial intelligence algorithm to develop fast, portable, and non-invasive intelligent Raman spectroscopy analysis and detection equipment for oral cancer diagnosis. Optical fiber Raman spectroscopy was used as an oral tissue data acquisition method to construct an extensive data set of oral tissue Raman spectroscopy, combined with deep learning algorithm to establish the oral tissue attribute identification model. Furthermore, the deep learning model was optimized and deployed to edge computing devices with high accuracy.

Preoperative intelligent diagnosis of early oral mucosal lesions and cancer tissues with high sensitivity and high specificity is helpful for timely and accurate diagnosis of oral cancer tissues in patients. This project has successfully accepted the Frontier Projects of Beijing Natural Science Foundation-Haidian Joint Innovation Fund in December 2021 and has been recognized by many professionals from well-known international and domestic research institutions.

This project is likely to improve the diagnosis and screening level of oral cancer, contribute to the early detection and early treatment of oral cancer patients, improve the survival rate and survival status, and promote the clinical application of Raman spectroscopy. The Raman spectroscopy equipment for in-vivo detection of oral cancer based on artificial intelligence will fill the gap of non-invasive oral cancer diagnosis technology in China.

Development of a novel cytokine product based on NAD⁺ regulation for treating aging-related sarcopenia

Principal Investigator	Jun Li, PhD
PI Primary Affiliation	Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences
Co-Investigator(s)	Zheng Wang, PhD; Xiaoqian Zhang, PhD; Na Liang, PhD; Qing Tan, MD; Wenbin Liu, BS

PROJECT DESCRIPTION

Aging is one of major factors that account for skeletal muscle mass loss and dysfunctions. So far, there is no practically efficient method to ameliorate skeletal muscle degeneration caused by aging. Supplementing NAD⁺ is a newly emerging strategy that has shown promising effects in slowing down aging-related muscle dysfunctions. The previous work of our team showed that increasing NAD⁺ in naturally aged mice or premature aging mice model by injecting NMN had improved muscle functions, yet which were not reproduced in C2C12 cells if directly adding NMN into the culture media. Based on this, we hypothesize that NAD⁺ ameliorates age-related muscle dysfunctions by regulating the secretion of adipokines in vivo. In this project, we first identify the key factor secreted by adipose tissues as SPN, which is responsible for the beneficial effects in muscles due to NMN injection; and then uncover the mechanism by which this key adipokine under the influence of NAD⁺ regulates

the metabolism and fiber types remodeling of skeletal muscles, along with dissecting the signal pathways involved; subsequently, we verified the therapeutic effect of improving muscle functions by supplementing this particular adipokine in naturally aged mice and Sarcopenia mice model; finally complete the clinical verification of the correlation between SPN and sarcopenia. This project reveals the very first evidence for the inter-tissue crosstalk between muscle and adipose mediated by NAD⁺ and provides a new option for sarcopenia therapeutic intervention.

Development of a novel self-assembled defense peptide hydrogel for the treatment of oral mucosal healing disorders after chemotherapy

Principal Investigator	Yuxing Guo, PhD
PI Primary Affiliation	Peking University Hospital of Stomatology
Co-Investigator(s)	Xuehai Yan, PhD; Qingxiang Li, PhD; Guizhi Shen, PhD ; Ruirui Xing, PhD

PROJECT DESCRIPTION

Bone metastases are often occurred in patients with advanced tumors, and medication-related osteonecrosis of the jaw (MRONJ) is likely to occur once anti-angiogenic and/or anti-resorptive drugs are used for a long time. Surgery is a common method for the treatment of MRONJ, but oral mucosal is prone to have healing disorders after the application of anti-angiogenic drugs. How to reduce local inflammation in the oral mucosa and promote wound healing without interfering with the chemotherapy process has become a major clinical problem for cancer patients.

Host defense peptides are an emerging class of modulators involved in innate immunity. They mediate the migration of monocytes and leukocytes to the site of tissue damage, and regulate pro- and anti-inflammatory responses through TLR or C-type lectin receptors. However, when host defense peptide molecules are directly applied in vivo, there are still shortcomings such as short half-life, low efficiency, and easy degradation. The positive charges in the new-designed supramolecular self-assembled hydrogels can respond to the negatively charged surfaces in the microbial environment, so that they can function through slow disassembly, with the advantages of slow release, resistance to degradation, enhanced immune regulation, and long-lasting anti-microbial.

Based on our research work in the development of oral mucosal healing model after chemotherapy and peptide self-assembly mechanism, this project plans to design and select specific host defense peptides and focus on research of its self-assembly and immune regulation process, and the feasibility of its future clinical application to improve oral mucosal healing capability after chemotherapy.

Environmental Risk Factors and Successful Aging: Environmental Exposome Systematic Study

Principal Investigator	Qun Xu, PhD
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Co-Investigator(s)	Meiduo Zhao, PhD Jing Xu, PhD Ang Li, PhD Yayuan Mei, BS Quan Zhou, BS Jiaxin Zhao, MS

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PROJECT DESCRIPTION

Healthy China keeps our new working goal. A healthy elderly population is a top priority in building the beautiful China, especially at a time when we are faced with a rapidly growing proportion of the elderly population. Therefore, it proves an urgent action to explore effective environmental interventions to promote the health of the elderly population as well as reduce the disease burden especially caused by non-communicable diseases.

Our team want to reveal the effects of multiple environmental exposures (air pollution, heavy metal, OPEs and PFAS) on health outcomes (cognitive ability, CVDs, telomere length, disability) and to provide population-based epidemiological evidence for the development of environmental control policies.

We hope to achieve the following expected project results: Set up a system to evaluate the environmental exposure and health effect from the perspective of exposome; and further, provide a series of new policy recommendations for the control and prevention of environmental pollution based on current pollution and control strategy.

Establish "tertiary hospital-community-home" palliative care informationization management system based on compact medical consortium

Principal Investigator	Jin Gu , MD
PI Primary Affiliation	Peking-Tsinghua Center for Life Sciences, Peking University,
Co-Investigator(s)	Xiaodong Wang , MD/PhD;

PROJECT DESCRIPTION

At present, China has entered an aging society, and the incidence of chronic diseases such as cancer and cardiovascular diseases has been on the rise. Providing patients with full-cycle comprehensive physical and mental care directly affects their lives and quality of life. Palliative care is the multi-faceted and humanistic care for patients at the end of life, which aims to help patients pass away comfortably, peacefully and with dignity. However, China's palliative care work started late, the development is not balanced, the number of beds in tertiary hospitals can not meet the growing needs of terminal patients. Therefore, how to promote the popularization of palliative care work in grass-roots communities is particularly important. This project aims to establish a replicable and popularizable "tertiary hospital-community-home" joint management model based on Internet information platform. Based on the existing palliative care center and community compact medical consortium system in our hospital, we plan to build a "tertiary hospital-community-home" palliative care combined care model from the following aspects : (1) further improve the construction of tertiary hospital palliative care center multidisciplinary platform; (2) Strengthen professional training in palliative care for community medical staff; (3) Establish community hospice service stations; (4) Establish of hospice beds at home; (5) Construct tertiary hospital-community-home palliative care information platform. The project will eventually establish a comprehensive care model based on the Internet platform that integrates the participation of internal medicine, surgery, traditional Chinese medicine rehabilitation, nutrition, psychology, pain, nursing and other multidisciplinary participation.

Exploration of Individualized Skull Base Reconstruction Strategy for Endoscopic Skull Base Tumor Surgery with the Goal of Fast Recovery

Principal Investigator	Pinan Liu, MD
PI Primary Affiliation	Department of Neurosurgery, Beijing Tian Tan Hospital, Capital Medical University, Beijing, China
Co-Investigator(s)	Peng Li, MD; Zhijun Yang, MD; Bo Wang, MD; Xingchao Wang, MD; Zhenmin Wang, MD.

PROJECT DESCRIPTION

With the aging trend becoming more and more obvious, skull base tumors have been found in more and more elderly people. Traditional craniotomy for resection of skull base tumors is traumatic and the therapeutic effect is not ideal. In the past 20 years, endoscopic technology has developed rapidly in neurosurgery, which can remove skull base tumors with minimal trauma and greatly reduce surgical trauma. After the operation, reliable skull base reconstruction is needed to properly protect the exposed skull base blood vessels and nerves, while tightly sealing the skull cavity to prevent postoperative cerebrospinal fluid leakage and intracranial infection. This is a critical step in endoscopic skull base surgery. At present, due to the limitation of surgical strategy, technique, equipment and material, the effect of skull base reconstruction in endoscopic surgery is not satisfactory, which is an important reason for serious postoperative complications and affecting the smooth rehabilitation after surgery. Systematically improving the level of endoscopic skull base reconstruction is the key to further improve the level of endoscopic skull base surgery. This project intends to establish a complete endoscopic skull base reconstruction system, improve the curative effect of endoscopic skull base surgery, reduce surgical complications and promote the rapid recovery of patients through (1) exploring and developing new skull base reconstruction technology represented by endoscopic skull base dural suture, (2) developing new skull base reconstruction instruments and materials, and (3) establishing and popularizing individualized endoscopic cranial base reconstruction strategies.

Fully digital complete denture restoration technology guided by intelligent facial virtual prediction

Principal Investigator	Fusong Yuan, PhD, DDS
PI Primary Affiliation	National Engineering Research Center of Oral Biomaterials and Digital Medical Devices; Research Center of Engineering and Technology for Digital Dentistry, Ministry of Health
Co-Investigator(s)	Yuchun Sun PhD, DDS; Li Ma, PhD; Shanshan Liang PhD, DDS; Xinyue Zhang, MS

PROJECT DESCRIPTION

With the aging of the population, the number of edentulous patients is increasing year by year in our country. The edentulous arch seriously affects the patient's chewing, pronunciation and aesthetic functions, and even leads to systemic diseases such as the digestive system, causing trauma to the patient's body and mind.

Complete denture is a routine restorative treatment for edentulous patients. At present, manual operation is mainly used in clinical practice. Usually, it is accompanied by some side effects, including pain, poor chewing function, poor pronunciation, poor aesthetic effect and other problems.

In order to solve the above problems, the project team organically applied the current advanced artificial intelligence technology and digital technology to complete denture restoration, and then proposed the concept of fully digital complete denture restoration under the guidance of intelligent facial virtual prediction. The main technical solutions are as follows:

- (1) The facial appearance of patients with teeth can be predicted from the facial appearance without teeth by leveraging deep learning technologies;
- (2) Based on the predicted facial appearance, the intelligent design of the complete denture can be carried out;
- (3) Complete denture can be made automatically and accurately through CAM or 3D printing technology and equipment.

This project can realize virtual prediction of normal facial appearance of edentulous patients, digital establishment of occlusal relationship, and digital design and production of complete dentures, shortening the restoration time. This project can improve the quality of repair, restore the physical and mental health of patients, which has important clinical application value.

Innovative improvements in the mechanical microenvironment for the treatment of age-related knee osteoarthritis

Principal Investigator	Aifeng Liu, MD
PI Primary Affiliation	The First Teaching Hospital of Tianjin University of Chinese Medicine
Co-Investigator(s)	Aifeng Liu, MD; Juntao Zhang, MS; Chao Zhang, MD; Yuandong Li, MS

PROJECT DESCRIPTION

Knee osteoarthritis (KOA) is a common joint condition characterized by gradual cartilage loss, subchondral bone remodeling, and synovial inflammation, resulting in symptoms such as persistent pain, joint stiffness, and physical and psychological problems. Over the last two decades, over 250 million people have been diagnosed with KOA, with the global incidence increasing considerably. The condition has a significant impact on patients' quality of life and imposes a significant burden on society and the economy.

In the previous study, a musculoskeletal model of knee OA was constructed following clinicopathological characteristics. In this project, the non-linear characteristics of the stress distribution in the knee "tendon" and "bone" were identified, and the steady-state damping characteristics of the cartilage repair microenvironment were clarified. This project carried out a new strategy of solid lubrication and stress regeneration. This project uses biomechanical testing, and reverse engineering techniques to construct simulation models and evaluate 3D graphene oxide nano scaffolds and Xianlingbao and Epimedium-containing serum to develop an umbilical-derived MSC-regulated joint mechanics microenvironment. The nano scaffold and drug-containing serums were loaded on an animal model to evaluate the extent of cartilage repair using biochemical, pathological, gene expression and gait analysis. Combined with the biological coupling theory, the mechanical microenvironment homeostasis was demonstrated, and the 3D graphene oxide nano scaffold and Xianlingbao and Epimedium-containing serum were used to cultivate the mechanical microenvironment characteristics and cartilage repair mechanism of the umbilical cord-derived MSC, contributing to quantitative diagnostic evidence and qualitative treatment ideas for the clinical diagnosis and treatment of KOA.

Quantitative measurement of brain state and neurofeedback intervention techniques for the treatment of perioperative neurocognitive disorders in elderly patients

Principal Investigator	Hui Zheng, PhD, MD
PI Primary Affiliation	National Cancer Center, National Clinical Research Center for Cancer, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College
Co-Investigator(s)	Yibing Wu, B.E.; Jie Yu, PhD, MD; Cheng Ni, PhD, MD; Yongfeng Cheng, B.E.;

Wenyue Xu, M.A.; Huaqing Chu, MD; Qi Hou, PhD, MD

PROJECT DESCRIPTION

The incidence of perioperative neurocognitive disorders (PND) in elderly surgical patients are as high as 40%. PND is closely related to the decline of postoperative quality of life, long-term cognitive impairment and increased one-year mortality after surgery. Current study and operation consider neuropsychological testing as the golden standard for the diagnosis of PND. However, results of such testing are often heavily dependent on factors such as types and judgment criteria for the assessment, and influences of aforementioned factors are magnified on elderly patients that have poor basic cognitive functions and compliance. Therefore, a rapid and objective test that quantitatively assess the brain status of such patients is urgently needed. In addition, there lacks clinical interventions that provide effective prevention or treatment for PND. EEG signals can reflect the comprehensive electrical activity of neurons in the cerebral cortex, and contain a large amount of human physiological, psychological and disease information that can assist the diagnosis and treatment of neurological diseases. With the continuous development of bioelectricity acquisition technology and artificial intelligence technology, the quantitative assessment of brain functional/emotional state and the data-guided brain health promotion training is in a technologically-ready state. Our project combined brain state quantification and neurofeedback training system to realize real time assessment and active intervention of perioperative brain function and status in elderly patients. Our study aims to achieve an integrated solution for the evaluation and improvement of perioperative brain state of elderly patients, reduce the incidence of PND, and provide insights for PND prevention and treatment.

Research and development of new drug loganin for the treatment of depression

Principal Investigator	Zhang Weiku, PhD
PI Primary Affiliation	China Japan Friendship Hospital
Co-Investigator(s)	Xu Jiekun, PhD; He Jun, PhD; Xia Congyuan, PhD;

PROJECT DESCRIPTION

Depression is a kind of affective mental disorder. The main physical symptoms in clinical manifestation are sleep disturbance. The marketed drugs have good antidepressant effects, however they cause easily sleep disorders and headaches, etc. Our team has discovered in recent years that loganin isolated from the traditional Chinese medicine *Cornus officinalis* has significant antidepressant effect. It has both sleep-promoting and analgesic effects. It was further found that loganin combined with fluoxetine can significantly shorten the onset time of fluoxetine. In addition, the results of toxicity studies in animals showed that loganin has no obvious toxic or side effects. If loganin is successfully developed, it will provide an innovative drug with high safety, definite antidepressant effect, and can improve sleep disorders in patients with depression.

Risk prediction and scientific treatment strategy for atherectomy in colorectal cancer with thermofluidic multi-field bionic simulation intervention

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Co-Investigator(s)	Tang Dalian, PhD; Cheng Shikun, PhD; Cui Jian, PhD; Zhang Hui, PhD; Zhang Sizong, PhD; Feng Junxiao, PhD; Xu Wenrui, PhD; Zhao Zhinan, ME; Shi Kejian, ME; Zhong Liqiong, BE; Yang Gang, BE; Zhang Xinyi, BE; Liu Dinghai, BE; Shen Meng, BE; Zhu Lidong, BE; Chen Xingli, BE; Zheng Qiang, BE; Fan Huanbao, BE.

PROJECT DESCRIPTION

While colorectal cancer surgery is removed, the lymph nodes of the blood vessels need to be completely cleaned. Individualized characteristics such as lymph node distribution and tumor dominance of the intestinal tube will lead to the difference in diagnosis and treatment planning. Especially for elderly patients with poor basic conditions and diseases, they need to focus on planning and ligation plans to ensure intestinal blood supply to the anastomotic mouth, and prevent postoperative complications such as leakage and thrombosis. This project focuses on the mechanism of coupling of blood and blood vessels in the surgical environment/human temperature characteristics. A simulation model of multi-field coupling of fluid-thermal-solid in the colorectal blood supply system was established, which is used to simulate the planning of clinical surgery planning, risk assessment and postoperative transfer assessment. Before surgery, this project formulates the left/right half colon blood transport system model according to human characteristics parameters, mapping clinical symptoms, quantitatively portraying the blood supply system transportation mechanism, and clarifying the intestinal wall to support the vascular resection scheme. After surgery, the actual anastomotic blood flow of the left/right hemicolectomy patients is to be observed using fluorescent markers of the anastomotic blood supply, Doppler ultrasound blood flow monitoring and angiography, and the model is to be compared and analyzed with the predicted results and adjusted to provide scientific postoperative assessment and clinical treatment guidance to help patients recover efficiently.

Study of the anti-osteoporosis effect and mechanism of IMB-E0924G as a dual regulator for bone resorption and formation

Principal Investigator	Yanni Xu, PhD
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Co-Investigator(s)	Shuyi Si, PhD

PROJECT DESCRIPTION

With the extending lifespan and accelerating population ageing, osteoporosis (OP) has become a major health problem affecting life quality and lifespan in elderly population. The side effects and limitations of existing osteoporosis drugs including antiresorptive agents and anabolic agents affect its long-term application and compliance clinically. Efforts to develop small molecule drugs through inhibiting bone resorption and stimulating bone formation are critical to achieve normal bone turnover and bone dynamic balance and finally to improve the life quality of OP patients. Our research group have involved in the screening and discovery of novel anti-osteoporosis drugs. Previous studies have found compound E09241 can regulate OPG/RANKL and Wnt/ β -Catenin signaling pathway. Additionally, E09241 has been found to inhibit bone resorption and promote bone formation, and has potent antiosteoporosis effect in ovariectomized (OVX) rats. IMB-E0924G is derivative of E09241 obtained through structural optimization, which are highly potential to develop as novel antiosteoporosis drug due to its optimal pharmacokinetic and low toxicity. In this study, we will use molecular biology technology for the research on mechanism of IMB-E0924G in up-regulating OPG expression. Alizarin red staining, RNAseq, and other assays will be used to investigate the activity of IMB-E0924G in promoting osteogenesis and inhibiting osteoclast differentiation in vitro. Moreover, in vivo study will be conducted with OVX rats in order to study the antiosteoporosis effect. Furthermore, preclinical studies including pharmacokinetics, synthetic technology, and dosage form selection, will be conducted. The implementation of this project will finally obtain an anti-osteoporosis drug candidate with independent intellectual property right.

Study on novel drugs for the treatment of Alzheimer's disease based on epigenetic transcription with brain function recovery

Principal Investigator	Rui Liu, PhD
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Co-Investigator(s)	Zhuorong Li, MS; Guangzhi Shan, PhD; Ting Sun, PhD; Linjie Tan, MS; Li Zeng, MS; Zhongdi Cai, BS; Mimin Liu, BS; Kaiyue Zhao, BS

PROJECT DESCRIPTION

Alzheimer's disease (AD), the most common form of dementia, is becoming more prevalent due to the aging population and represents one of the grand challenges to human health and longevity. However, AD has neither achieved a clinical cure nor acquired a measure to control its deterioration. It is urgent to propose new treatment strategies. Our project team focuses on the frontier field associated with gene phenotypes in health and longevity, puts forward a new idea of multi-dimensional, spatiotemporal regulation mediated by non-coding genes, and develops new candidate drugs with a novel mechanism driven by the recovery of apparent transcription and brain function. Our previous research is the first to discover that lncRNA GAS5 and miR-23b-3p play key roles in the process of AD and are highly correlated with the cognitive impairment of AD patients. Furthermore, novel aryl vinyl leading compounds have been found to have neuroprotective effects against AD via the lncRNA GAS5/miR-23b-3p/target gene loop. Based on these novel findings, our project aims to perform a new round of structure optimization, therapeutic effects, mechanisms of action, and evaluation of early druggability of the aryl vinyl leading compounds against AD. To this end, we will achieve a new strategy in the treatment of AD, composed of a series of functional spatiotemporal targets and promising candidate drugs with the brand-new structure of aryl vinyl compounds and novel drug targets, thereby contributing to the scientific and technological strength in promoting health and longevity.

Supramolecular hydrogel drug delivery system for the synergy therapy of postoperative peritoneal metastasis and abdominal adhesion after cytoreduction surgery in the elderly colorectal cancer

Principal Investigator	Wang Ke, PhD
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Co-Investigator(s)	Dong Kai, PhD Li Qingqing, PhD Yang Fanli, MS Wen Jinpeng, PhD Liu Kailai, PhD Zhang Yuchen, PhD Gao Jushan, MS Zhao Xinxin, MS Hu Datao, MS

PROJECT DESCRIPTION

Tumor cytoreductive surgery is a common method for the treatment of colorectal cancer in the elderly, but it is not only prone to adhesions after the operation, leading to chronic pelvic pain, intestinal obstruction, and other complications. Residual tumor cells may also cause tumor recurrence or peritoneal metastasis, resulting in surgical treatment failure. Previous studies have shown that peritoneal mesothelial-mesenchymal cell transition (MMT) plays a key role in the pathogenesis of peritoneal adhesions and tumor peritoneal metastasis, and inhibition of MMT has become a new target for simultaneous anti-cancer and anti-adhesion therapy. Based on previous research, this project is based on the design idea of transforming factor TGF- β 1 promoting the process of MMT, focusing on the key links of MMT in peritoneal adhesion and tumor peritoneal metastasis, and intends to prepare an ultra-soft, self-fusing and hydrogen-bonded crosslinked supramolecular hydrogel with highly controllable mechanical properties and construct a nanoparticles@hydrogel drug delivery system to co-deliver TGF- β 1 siRNA and anti-tumor drugs. It is expected that the hydrogel itself exerts a barrier function to prevent adhesion, while effectively delivering nanoparticles locally, and further evaluates the efficacy of the drug delivery

system to achieve simultaneous anti-cancer and anti-adhesion therapy in the animal model of postoperative adhesion and tumor peritoneal metastasis, and the mechanism of the drug delivery system is thoroughly probed on the cellular and molecular biological level, providing new ideas for the prevention of adhesions and tumor metastasis after tumor cytoreduction in the elderly.

Synthesis and assessments of thermoplastic polyurethane elastomer--the basic material applied in cardiovascular prosthesis for the aged.

Principal Investigator	Chenxi Ouyang , PhD
PI Primary Affiliation	Deputy director of Vascular Surgery, Fuwai Hospital
Co-Investigator(s)	Xia Dong , PhD ; Ping Zhu , PhD ; Yilang Qin M ; Ke Zhang M

PROJECT DESCRIPTION

Cardiovascular disease is one of the major medical burdens faced by our aging society in the future. Artificial replacement implants (such as artificial blood vessels and prosthetic valves) are important consumables in surgical treatment. Among them, TPU elastomers are widely used because of their good biocompatibility and mechanical properties. This study combined the Chinese Academy of Sciences institute of chemical engineering plastic key laboratory, cardiovascular state key laboratory, wuhan yeung sum biological co., LTD., ningbo BeiAng co., LTD., through university-industry cooperation mode of TPU elastomer processed into artificial blood vessels and valves and other downstream products from learn the formula design of biomedical polymer chemistry and materials and performance verification.

The pre-clinical study of a novel diuretics S3-F for the treatment of hyponatremia

Principal Investigator	Baoxue Yang, MD, PhD
PI Primary Affiliation	Peking University
Co-Investigator(s)	Min Li, PhD; Yue Xu, PhD; Shuyuan Wang, PhD; Hang Zhang, MS; Yi Ying, MS; Nannan Li, MS.

PROJECT DESCRIPTION

Previous studies of our group have shown that urea transporters (UT) play a very important role in the mechanism of renal urinary concentration. The inhibition of UT activity can block the intrarenal urea cycle, reduce capacity of urine concentration, and produce urea-selective diuresis. This project intends to establish the syndrome of inappropriate antidiuretic hormone secretion (SIADH) model, aortic constriction induced heart failure model and bile duct ligation induced cirrhosis ascites model, to explore the therapeutic effect of UT inhibitors on hyponatremia and its mechanism. Then carry out systematic preclinical pharmacodynamic and pharmacokinetic studies on this new diuretic, and confirm the target using UR knockout animal models. The final experimental results will support the scientific hypothesis that UT inhibitors can be used as new medication for hyponatremia. Also, non-clinical research reports will be generated for investigational new drug application. Our group found the first UT-specific inhibitor with oral diuretic activity-diarylamide compound S3-F (human UT IC₅₀=0.08 μM), with diuretic effect (rat urine volume increased by 2 times, osmotic pressure decreased by 10 times, diuretic effect lasted for 8 hours), without affecting excretion of Na⁺, K⁺ and Cl⁻, less toxic side effects (high oral doses in mice do not show toxicity). The preparation process of S3-F is mature (6 steps, with an overall yield of 25%~30%, and the process can be scaled up for production). S3-F is expected to be developed into a First-in-class novel diuretic without affecting electrolyte balance for the treatment of hyponatremia.

The 'Eat More' Peptide IMM-H029, a Class 1 Medicine, for the Treatment of Lung Interstitiopathy

Principal Investigator	Xiaoxi Lv, PhD
PI Primary Affiliation	The Institute of Materia Medica, CAMS & PUMC
Co-Investigator(s)	Fang Hua, PhD; Shuang Shang, PhD; Bo Li, PhD; Jing Jin, PhD

PROJECT DESCRIPTION

Pulmonary interstitial diseases refer to changes in the structure of the pulmonary interstitium caused by different insults. It is characterized by pulmonary interstitial inflammation in the early stage, and then evolves into pulmonary fibrosis (PF) and vascular remodeling, and up to two-thirds of patients with interstitial lung disease have fibrotic changes. The lack of related research has led to extremely limited options for anti-fibrosis drug treatment. PF is mainly treated by anti-fibrotic therapy, inhibition of inflammation, antioxidant therapy, and acid suppression therapy. There are only two FDA-approved drugs for the treatment of PF, pirfenidone and nintedanib. However, except for lung transplantation, existing drugs can only relieve the symptoms of PF but cannot reverse the fibrotic changes. At present, almost all anti-PF drugs are developed to inhibit the activation of fibroblasts and the inflammatory response. However, most patients with PF have already formed fibrotic change at the time of diagnosis. Therefore, it is urgent to develop drugs that can clear the collagen deposited in lung tissue. We previously developed an autophagy-activating polypeptide IMM-H029 that promotes the degradation of the collagen through autophagy pathway, which can effectively attenuate PF induced by various factors in many animal models with excellent safety. The purpose of this project is to complete the preclinical study of IMM-H029. The research and development of IMM-H029 not only fills an important gap in the field of PF drug treatment, but its combination with anti-inflammatory and traditional anti-fibrotic drugs will also bring new benefits to patients with PF.

Ways to Improve and Control the Degradation of the Electrospun Chitosan membrane, A Guided Bone Regeneration Membrane

Principal Investigator	Hengjie Su, PhD
PI Primary Affiliation	Chinese Academy of Medical Sciences
Co-Investigator(s)	Xiang Ji, PhD; Bowen Zhang, PhD; Shuo Meng, MD

PROJECT DESCRIPTION

Periodontitis is the 11th highly prevalent disease all over the world. It is the major reason of tooth lost. One of the periodontal treatments is to reconstruct the alveolar with the guided bone regeneration (GBR) membrane and the bone graft. The most clinical used GBR membranes are collagen membranes. However, they have disadvantages of low suture strength and being easily infected. Hence, it is urgent to have new membranes that are more reliable. Electrospun chitosan membranes that were treated with new post-treatment showed biocompatible, biodegradable and antibiotic properties, that were expected to be the next generation of the economic GBR membrane. Besides, they showed better mechanical strength and bone growth assistance than some commercialized GBR membranes. In a previous animal study, some chitosan membranes showed too fast degradation rates to fully cover the defect area during the bone reconstruction, that was the main obstacle to commercialize the chitosan membrane. In this research, two crosslinkers, genipin and Na₂HPO₄, will be chosen to crosslink the electrospun chitosan membrane to increase the structure connections and decrease their degradation rates. This proposal is expected to overcome the difficulty of controllable stable degradation for the electrospun chitosan membrane, that makes the clinical application become possible. It will also enable the future of providing quality periodontal treatments for most patients.