

HEALTHY LONGEVITY GLOBAL COMPETITION

2025 Catalyst Awardees

Sponsor: Research Grants Council of the Hong Kong Special Administrative Region, China

AI Driven Novel Cancer Pain Targeted Therapy

Principal Investigator	Patrick Ming Kuen TANG, PhD
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Co-Investigator(s)	Xiaohua Jiang, PhD (The Chinese University of Hong Kong); Dongmei Zhang, PhD (Jinan University); David J Nikolic-Paterson, PhD (Monash University)

PROJECT DESCRIPTION

Pain is common in patients with advanced cancer, which results in poorer life quality as well as overall survival. However, cancer pain is unique and low response to all available treatments, its effective therapeutic strategy is still an unmet need in the clinics.

Recently, by better understanding cancer microenvironment at single-cell resolution, we discovered a new phenomenon “Macrophage to Neuron-like cell Transition” (MNT) as the key mechanism for cancer pain formation. We demonstrated that genetic depletion of MNT effectively prevents cancer pain in animal models, representing a novel therapeutic target for the clinical cancer pain. More importantly, by using AI drug discovery system, our preliminary works identified an FDA approved compound can prevent MNT in vitro, implying its clinical potential for the cancer pain.

In this project, we will optimize this novel MNT inhibitor into a clinical compatible therapy for the cancer pain. Its efficacy and safety will be evidenced by using our well-established cancer pain models in vitro and in vivo, where the underlying working mechanism will be further defined with our advanced single-cell bioinformatics at molecular level. The project findings will be impactful and clinically applicable and serve as important rationales for translating our benchtop discovery of MNT into effective clinical solution to improve the well-being and longevity of cancer patients.

Development and Application of a real-time, location-based heat health warning system for older adults

Principal Investigator	Hung Chak Ho, PhD
PI Primary Affiliation	Department of Public and International Affairs, City University of Hong Kong
Co-Investigator(s)	Eric Lai, PhD; Cui Guo, PhD

PROJECT DESCRIPTION

Heat health risk in older adults has been widely observed. If there are no adaptations in the future, the return periods of fatal heat events will be shortened. Previous studies have applied heat health action plans to reduce

the health risk, such as heat health warning systems. However, the effectiveness can be inconsistent. The reason for the failure of these studies may be that there are no real-time heat health warnings at the individual-level and no detection/prediction based on personal condition (e.g., heart rate, body temperature). Since heat health warnings are usually city or community-level interventions, older adults may not have sufficient heat-related knowledge, attitudes, and practices (KAPs), health literacy and disaster awareness for health prevention. Therefore, a tool is needed that provides an individualized warning system based on personal condition (e.g., physiological responses) and offers health prevention information with the potential to increase health literacy. This study aims to develop real-time interventions targeting heat-related health risks in older adults. Using mobile sensing technologies, heat risk can be estimated based on the individual's condition (e.g., heart rate, body temperature). The warning system developed based on the individual's condition can provide real-time signals to prevent heat-related health risks. The use of location-based apps can help increase health literacy and heat awareness among older adults and ultimately improve older adult's self-care abilities in dealing with heat waves. This can improve healthcare management by reducing excess morbidity/mortality in older adults.

Development of a mouse-human xenograft neuronal model for the study of aging and age-related diseases

Principal Investigator	Kwok-On Lai, PhD
PI Primary Affiliation	City University of Hong Kong
Co-Investigator(s)	Ralf Jauch, PhD

PROJECT DESCRIPTION

Patient-derived induced pluripotent stem cells (iPSCs) provide a promising tool to understand human brain disorders and develop personalized medicine. However, iPSCs become rejuvenated after reprogramming and cannot recapitulate the essential features of age-associated neurodegeneration. Human induced neural stem cells (hiNSCs) represent an attractive alternative because they avoid the detour to pluripotency, thereby carrying age signatures of the donors. Nonetheless, their use to mimic an aging neuronal model in vivo has not been attempted. Establishing a human stem cell-based neuronal aging model would be enormously useful for testing therapeutic interventions in late-onset dementia such as Alzheimer's disease, which is characterized by the loss of synaptic connections. Here we will genome-edit hiNSCs from donors of young and old individuals to express fluorescent protein and aging markers, and then transplanted them into mouse brain for better synaptic maturation in a physiological environment. Chronic restraint stress will be applied to the mice to induce aging-associated cellular processes in the brains. We will further test our aging model by addressing whether exercise and caloric restriction of the mice attenuate aging of the grafted human neurons. This novel human-mouse chimeric model can provide an unique opportunity for future assessment of how drug candidates and life style adjustments (exercise, diet, probiotics) act at the systemic level to slow down neurodegeneration of human neurons.

Glycohemoglobin Quantitative Rapid Test for Screening and Management of Diabetes

Principal Investigator	Ting-Hsuan Chen, PhD
PI Primary Affiliation	Department of Biomedical Engineering, College of Biomedicine, City University of Hong Kong
Co-Investigator(s)	Yao Lu, RN

PROJECT DESCRIPTION

Diabetes is a public health problem with >10% of global prevalence. It is asymptomatic in the early stages and self-propelling, so often diagnosed in the later, incurable stages. To screen and manage diabetes, glycated

haemoglobin (HbA1c) level, which integrates glucose levels over the receding 6–8 weeks, was recommended to replace standard glucose tests to avoid acute perturbations due to activity, stress, and drugs. However, its quantitative measurement is costly and challenging.

The COVID-19 pandemic has popularized the use of rapid tests to attenuate the time-consuming and complicated re-examination in the hospitals, demonstrating at-home self-screening as the future of health services. Can the concept of at-home self-tests be repurposed to diabetes management? Unfortunately, conventional rapid tests are only for yes/no and unable to give the HbA1c level. On the other hand, while in-vitro diagnostic devices (IVDs) for quantitative measurement are widely available, they are often too expensive for home use.

Here, we propose a quantitative rapid test to determine HbA1c levels. The tests include a disposable microfluidic device and a mobile app. It automates specimen sampling after dipping fingerstick blood. Without the need for external devices, the HbA1c levels can be converted into visible bar lengths displayed on the microfluidic device, enabling results quantification recording through a mobile app. This all-in-one, self-contained detection kit eliminates the need for external devices, offering rapid, simple, affordable, and quantitative detection. As a novel medical solution, it will provide large-scale screening and self-management for diabetes patients beneficial to our aging society.

Investigating the impact of exercise-inducible metabolites on physiological ageing

Principal Investigator	Wong Hoi Leong Xavier, PhD
PI Primary Affiliation	Hong Kong Baptist University
Co-Investigator(s)	Asthana Pallavi, PhD

PROJECT DESCRIPTION

Senescent cells are closely linked to aging and age-related disorders, making them promising targets for anti-aging therapies. Therapies targeting senescent cells (SnCs) fall into two main categories: senolytics, which eliminate SnCs, and senomorphics, which suppress pathological senescence-associated secretory phenotype (SASP). These approaches have shown benefits in aging and related diseases, such as extending lifespan, reducing inflammation, and enhancing cognition. However, they have limitations. Senolytics can effectively remove SnCs when they are few, but as SnCs increase with age, their elimination might cause significant tissue damage and impair organ function. Senomorphics, while rejuvenating, can hinder immune surveillance of pathogens and cancer cells. Therefore, developing new strategies to target SnCs is essential to overcome these challenges.

Regular physical activity positively influences the aging process, though the exact molecular mechanisms remain unclear. Our preliminary study found that L-lactate-derived metabolite N-lactoyl-phenylalanine (Lac-Phe), an exercise-induced anorexigenic signaling molecule, can reverse senescence by restoring the proliferative capacity of senescent cells (SnCs). In a mouse model of progeria, a rare genetic disorder that accelerates aging, Lac-Phe treatment reduced SnCs, promoted rejuvenation, and resulted in extended lifespan, improved physical performance, and reduced aging markers without any undesirable tumorigenic and toxic effects. In this proposal, we will further explore the anti-ageing potential of Lac-Phe in physiological ageing. We will investigate the impact of Lac-Phe treatment on age-related functions, such as physical performance, cognitive function and cellular senescence, in naturally aged mice. This study will offer a potential applicable and feasible therapeutic approach to mitigate senescence-related pathologies and ageing.

New-Generation Ear-Based Devices for Ambulatory Cardiovascular Health Monitoring

Principal Investigator	Ni ZHAO, PhD
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PI Primary Affiliation	Department of Electronic Engineering, The Chinese University of Hong Kong
Co-Investigator(s)	Shirong Qiu, PhD; Shun Wu, PhD candidate

PROJECT DESCRIPTION

Cardiovascular diseases (CVDs) are a leading cause of morbidity and mortality worldwide, necessitating innovative solutions for continuous health monitoring. This proposal builds on our existing achievements in wearable sensors and physiological monitoring to develop a new-generation ear-based devices for ambulatory cardiovascular health monitoring, offering a novel and effective approach to track cardiovascular metrics in real-world settings. The device integrates advanced optoelectronic technologies into an ear-mounted form factor, enabling non-invasive, real-time monitoring of vital signs such as blood oxygen saturation, blood pressure and arterial stiffness.

The unique advantage of placing the sensing unit at the ear lies in its close proximity to key vascular regions, such as the auricular and temporal arteries, which provide strong and stable signals for accurate physiological measurements. Compared to other body locations, the ear offers a superior balance of signal reliability, user comfort, and practicality for long-term monitoring. Furthermore, many older adults, a population particularly vulnerable to cardiovascular diseases, are already accustomed to wearing ear-based devices, such as hearing aids. The proposed sensing module is designed to be so compact that it can be directly integrated into a hearing aid, combining health monitoring with an existing, familiar device to encourage widespread adoption.

This device has broad applications in preventing, diagnosing, and managing CVDs, such as monitoring hypertension, arrhythmias, and early signs of heart failure. It is ideal for high-risk populations, such as older adults and individuals with chronic conditions, and supports proactive health management, early detection, and timely intervention to improve patient outcomes.

Nose-to-Brain Delivery of A β -targeting Nanotheranostics for Early Intervention in Alzheimer's Disease

Principal Investigator	Shing Fung Chow, PhD
PI Primary Affiliation	The University of Hong Kong
Co-Investigator(s)	Raymond Chuen Chung Chang, PhD

PROJECT DESCRIPTION

Alzheimer's Disease (AD), characterized by amyloid-beta (A β) and tau pathologies, stands as the predominant manifestation of dementia. The escalating AD prevalence attributed to an aging population poses substantial socioeconomic burdens. Early AD intervention is crucial but hindered by the lack of diagnostic tools for asymptomatic stages and the inadequacies of existing treatments, which fail to halt disease progression and possess safety concerns. There is a pressing need for innovative dual-function diagnostic and therapeutic modalities (theranostics) for AD management. We previously developed curcumin-conjugated superparamagnetic iron oxide nanoparticles (CUR-SPIONs) for intravenous administration, targeting A β oligomers as MRI contrast agents for early AD diagnosis. This project aims to promote healthy longevity by expanding their application to theranostics, integrating diagnostic capabilities with on-demand magnetic hyperthermia for A β disaggregation. We propose engineering CUR-SPIONs into nasal powders for nose-to-brain delivery, thereby enhancing brain targeting, improving MRI detection sensitivity, and minimizing systemic side effects. To test our hypotheses, we will create and optimize CUR-SPION nanoagglomerate nasal powders using an in-situ thermal gelation and spray-drying technology platform. The A β -targeting efficiency in vivo will be assessed through MRI imaging and immunohistochemistry following intranasal powder administration. Finally, the therapeutic efficacy of CUR-SPION-facilitated mild magnetic hyperthermia will be evaluated in transgenic AD mice using behavioral tests, MRI imaging, and immunohistochemistry. Successful completion of this project could revolutionize AD treatment by offering a simple, non-invasive method to deliver theranostics directly to the

brain. Our idea could significantly enhance early AD management and promote healthy longevity, transforming the landscape of AD care.

Precision Delivery of Transcranial Focused Ultrasound for Essential tremor in the Elderly

Principal Investigator	Nicholas Xuanlai Fang, PhD
PI Primary Affiliation	Department of Mechanical Engineering
Co-Investigator(s)	Erqian Dong, PhD; Xiaochuan Wu, PhD; Bomin Sun, MD, PhD; Halmurat Parhat, MD

PROJECT DESCRIPTION

Essential tremor, common among the elderly, significantly affects motor function and quality of life. This proposal focuses on a promising non-invasive treatment using transcranial focused ultrasound (TCFUS) to stimulate the Central Lateral posterior nucleus. Current treatment options, such as thalamic electrode implantation and radiofrequency ablation, are invasive and high-risk for elderly patients, while ultrasound remains the only non-invasive, non-craniotomy method. One major challenge identified by neurosurgeons is that low skull bone density often reduces the effectiveness of TCFUS by disrupting the way ultrasound waves propagate and focus. To solve this, we propose an adaptive CT-guided soft metalens system for precise and personalized TCFUS treatment. This system combines CT imaging with advanced machine learning (Fully Convolutional DenseNets, or FC-DenseNets) to accurately map skull structure and bone density. It uses customizable, soft, ultrathin metalenses made of biocompatible materials that dynamically adjust ultrasound wavefronts. This ensures that the waves can compensate for skull density variations and accurately target the affected brain areas. By providing real-time bone density mapping, the system optimizes ultrasound delivery, improving precision, minimizing energy loss, and reducing unwanted side effects. Initial testing will demonstrate its ability to maintain high accuracy under different skull conditions. Future trials will assess its safety and effectiveness in elderly patients with essential tremor. This innovative soft metalens technology aims to overcome current limitations, offering a safer, personalized, and effective solution for non-invasive brain therapy.

Targeting the Heart: Nanoparticle Drug Carriers for Innovative HFpEF Therapy

Principal Investigator	Yin CAI, PhD
PI Primary Affiliation	Department of Health Technology and Informatics, The Hong Kong Polytechnic University
Co-Investigator(s)	Chun Yuen Alex WONG, PhD; Zhe YANG, PhD; Chang LIU, PhD; Wensheng QI, PhD

PROJECT DESCRIPTION

As the global population ages, heart failure with preserved ejection fraction (HFpEF) presents a growing and formidable health challenge, particularly for the elderly. This condition is characterized by a stiffened heart that cannot properly fill with blood, and current treatment options are severely limited. The pathophysiology of HFpEF is often driven by inflammation and oxidative stress, creating a complex therapeutic landscape. While certain natural cofactors can modulate these pathways, their clinical translation has been hindered by inherent instability and off-target effects. To overcome these barriers, our team has developed a novel nanoparticle-based delivery platform. This system utilizes a naturally derived, FDA-approved ingredient to transport a therapeutic agent specifically to the heart. This design protects the cargo from degradation, enhances its bioavailability, and concentrates its action precisely within cardiac tissue. The result is a targeted therapy that maximizes therapeutic potential while minimizing systemic exposure and adverse effects.

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Our compelling pre-clinical data demonstrates a significant reversal of key HFpEF symptoms. This project will now advance to comprehensive efficacy and safety testing. Our long-term goal is to translate this targeted nanotherapy through larger animal studies and into human trials, ultimately offering a transformative strategy to improve the quality of life and healthy longevity for patients suffering from HFpEF.