A*STAR and King's College London PhD Studentships October 2024 Entry

Contents

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When choosing a project from this catalogue in the funding section & research proposal section of the online application form, please enter the funding code that corresponds to the theme of your first project choice:

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2. Neuroscience and Mental Health: **THEME2_2024**
3. Biomedical Engineering and Medical Imaging: **THEME3_2024**

Important dates:

Application Stage	Date
Deadline for application	Sunday, 4 February 2024, 23:59 UK Time
Application Outcome	By 15 March 2024
Interviews	Week commencing 25 March 2024
Interview Outcomes	By 28 March 2024
Acceptance of studentship offer	By 14 April 2024
Degree Start Date	October 2024

The 2024/25 studentships will commence in October 2024. For further information or queries relating to the application process, please contact: doctoralstudies@kcl.ac.uk.

Projects listed in this catalogue are subject to amendments, candidates invited to interview will have the opportunity to discuss projects in further detail.

THEME1: Cells, Molecules and the Basis of Health and Disease

1.1 Leveraging recent advances in human genome annotations to identify structural variants associated with cardiometabolic phenotypes in diverse population groups.

Co-Supervisor 1A: Dr Mario Falchi

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Co-Supervisor 1B: Rajkumar Dorajoo and Professor Liu Jianjun (Mentor)

Research Institute: Genome Institute of Singapore

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https://www.a-star.edu.sg/gis/our-people/faculty-staff/members/jian-jun-liu

Project Description:

This research project aims to explore the genetic factors behind cardiometabolic diseases (CMDs) like heart disease, stroke, and diabetes. CMDs are leading causes of death globally and many of the genetic factors involved are still to discover, particularly among the so-called structural variants (SVs). SV are large-scale changes in the DNA, including deletions, duplications, or insertions of chunk of DNA, that can greatly impact health.

The project will use recent advancements in human genome studies that massively improve our ability of identifying SV in a human genome. The student involved in this project will analyse genetic data from diverse populations to understand how SVs affect cardiometabolic health.

Key activities include:

- Identifying SVs using advanced algorithms and recently generated pangenome reference data
- Detecting discordant SVs in identical twins to investigate the mechanisms underlying the appearance of novel SVs in the genome
- Using existing sequencing and health data from thousands of individuals from UK and Singapore to characterise SVs and investigate their involvement in CMDs

This research will enhance our understanding of the role of SV in CMDs, contributing to the identification of new genomic risk factors to improve prevention and treatment strategies.

The student will gain skills in genomics, bioinformatics, statistical analysis, and machine learning. They will also present their findings at major conferences and publish them in scientific journals.

The project is structured over four years and is a great opportunity for someone interested in genetics and health research to contribute to a significant field of study.

Two representative publications from supervisors:

Chang X, Gurung RL, Wang L, Jin A, Li Z, Wang R, Beckman KB, Adams-Haduch J, Meah WY, Sim KS, Lim WK, Davila S, Tan P, Teo JX, Yeo KK, M Y, Liu S, Lim SC, Liu J, van Dam RM, Friedlander Y, Koh WP, Yuan JM, Khor CC, Heng CK, Dorajoo R. Low frequency variants associated with leukocyte telomere length in the Singapore Chinese population. Commun Biol. 2021 3;4(1):519

Falchi M, El-Sayed Moustafa JS, Takousis P, Pesce F, Bonnefond A, Andersson-Assarsson JC, Sudmant PH, Dorajoo R, Al-Shafai MN, Bottolo L, Ozdemir E, So HC, Davies RW, Patrice A, Dent R, Mangino M, Hysi PG, Dechaume A, Huyvaert M, Skinner J, Pigeyre M, Caiazzo R, Raverdy V, Vaillant E, Field S, Balkau B, Marre M, Visvikis-Siest S, Weill J, Poulain-Godefroy O, Jacobson P, Sjostrom L, Hammond CJ, Deloukas P, Sham PC, McPherson R, Lee J, Tai ES, Sladek R, Carlsson LM, Walley A, Eichler EE, Pattou F, Spector TD, Froguel P. (2014) Low copy number of the salivary amylase gene predisposes to obesity. Nat Genet. 46:492-7

2.1 Digital fingerprinting of macrophage function during tissue regeneration and ageing using spatial transcriptomics and live cell imaging

Co-Supervisor 1A: Dr Robert Knight

Faculty: Faculty of Dentistry, Oral & Craniofacial Sciences

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Website: https://www.kcl.ac.uk/research/knight-group

Co-Supervisor 1B: Kok Hao Chen

Research Institute: Genome Institute of Singapore

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Website: https://khchenlab.github.io

Project Description:

The immune system is critical for health and wound healing. Macrophages are a key immune cell involved in wound healing and act at several stages, ranging from the remodelling of damaged tissue, through to controlling the formation of new cells. This involves a shift from an inflammatory phase to a repair phase, but it is not known which molecules control this process. A failure to regulate this transition of macrophage state is known to underlie a number of chronic diseases and aging conditions. To understand how macrophage transition is regulated this project aims to generate high resolution measures of which molecules are active in macrophages at the transition during wound healing and test their function and activity during aging.

Objectives include

1) identification of genes active in macrophages during tissue repair
2) functional evaluation of whether candidate genes regulate the transition from inflammation to resolution.

These will be achieved by identifying which genes are active in macrophages during repair and by showing if they are important for controlling macrophage function. Cell behaviour during regeneration will be visualised by fluorescent microscopy in transgenic zebrafish. Gene activity in macrophages will be measured in isolated cells and by visualising where genes are active in macrophages in the animal. This will identify genes which regulate macrophage transition during tissue repair and will be tested by manipulating their function in zebrafish. Understanding whether these genes are dysregulated during ageing would shed light on the critical role of the immune system in healthy ageing and during tissue repair.

Two representative publications from supervisors:

Robert Knight (Craniofacial and Regenerative Biology)
Brondolin, M., Herzog, D., Sultan, S., Warburton, F., Vigilante, A., Knight, R. D.

Migration and differentiation of muscle stem cells are coupled by RhoA signalling during regeneration Open Biology. 2023 Sep 13(9):230037 doi: 10.1098/rsob.230037

Kok Hao Chen (Spatial and Single-cell transcriptomics)
Goh, J. J. L.*, Chou, N.*, Seow, W. Y., Ha, N., Cheng, C. P. P., Chang, Y., Zhao, Z. W., Chen, K. H.
Highly specific multiplexed RNA imaging in tissues with split-FISH. Nature Methods, (2020)
https://doi.org/10.1038/s41592-020-0858-0.

3.1 Role of platelet and megakaryocytes in airway inflammation and their interactions with leukocytes in respiratory diseases

Co-Supervisor 1A: Dr Simon Pitchford

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Co-Supervisor 1B: Dr Anand Kumar Andiappan and Dr Olaf Rotzschke

Research Institute: Singapore Immunology Network (SIgN)

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Project Description:

Platelets have been recognized for some time to act as inflammatory cells in the defence of the body against infection, performing many functions normally associated with leukocytes. These roles are distinct from platelet function during haemostasis. Interestingly, platelets act as a 'bridge' between the innate and adaptive immune response. Platelets are activated in patients with asthma and are responsible for the misdirected inflammatory response. This can happen either through the intravascular recruitment and activation of inflammatory cells, such as as eosinophils and lymphocytes; but also the direct migration of platelets within lung tissue upon allergen sensitization and challenge to associate with lung dendritic cells (DCs), an event that was necessary for inflammatory responses upon subsequent, secondary allergen exposure. We outline a PhD programme to investigate how the process of antigen exposure affects platelet and MK 'molecular signature', intravascular and extravasular activity, and the development of immune memory. Future impact might lead to alternative strategies for 'disease modifying' therapies of allergic disease and provides an excellent basis for understanding host defence of respiratory pathogens in general as a next career step.

This exciting and ambitious project will allow the applicant to work in world-renowned laboratories at KCL and A*Star SIgN to learn in vivo disease models, human immunology, single cell RNA sequencing analysis, and clinical comparisons for relevance with patients with respiratory diseases such as asthma and AERD.

Overarching objectives are: 1. Characterize megakaryocyte (MK) and platelet involvement in antigen processing and development of airway inflammation; 2. To characterise the unique 'molecular signatures' of MKs and platelets with relevance to respiratory diseases; 3. To develop mouse models of airway inflammation in the context of disease pathophysiology.

Two representative publications from supervisors:

Shah SA, Kanabar V, Riffo-Vasquez Y, Mohamed Z, Cleary SJ, Corrigan C, James AL, Elliot JG, Shute JK, Page CP, Pitchford SC. Platelets Independently Recruit into Asthmatic Lungs and Models of Allergic Inflammation via CCR3. Am J Respir Cell Mol Biol. 2021; 64:557-568. doi: 10.1165/rcmb.2020-0425OC.

Lee WWL, Puan KJ, Lee B, Chua C, Koh SM, Yusof N, Tan KP, Luis BS, Ong J, Merid SK, Ang R, Chan XY, Hui LJ, Terenzani E, Lum J, Foo S, Zolezzi F, Yan ATS, Melen E, Yi SJ, Rotzschke O, Andiappan AK. Eosinophilic allergic rhinitis is strongly associated with the CD45RBlo subset of CD161+ Th2 cells that secretes IL-2, IL-3, IL-4, IL-5, IL-9, and IL-13. Allergy. 2023 Oct;78(10):2794-2798. doi: 10.1111/all.15846. Epub 2023 Aug 7. PMID: 37551093.

4.1 AI-Powered Discovery for Precision Immunology via Single-cell Data Science

Co-Supervisor 1A: Dr Sophia Tsoka

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Co-Supervisor 1B: Dr Jinmiao Chen and Dr. Li Xiaoli (Mentor)

Research Institute: Singapore Immunology Network

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Project Description:

New data types based on sequencing of single cells in tumours have the potential to transform cancer progression analysis and prognostic prediction. Despite their promise, single-cell data are large, sparse and represent complex molecular interactions. In this project we aim to capitalise on the availability of rich data resources at A*STAR that characterise immune repertoires across multiple cohorts and tissue types, and develop machine learning methodologies that can represent and mine complex data efficiently.

Tasks envisioned in this project include the implementation of knowledge graph frameworks to integrate multiple sources of input and provide flexible data management and mining. Machine learning models will be developed to include biologically informed deep learning models that incorporate prior knowledge based on known interaction events, and the use of graph neural networks to represent and analyse patient immune history via immune repertoires for accurate prognosis prediction. In addition, foundation models trained on large datasets will be used to improve the annotation of cell types and uncover new biomarkers and drug targets.

Through the above tasks the student will obtain experience on developing cutting-edge machine learning methods for biomedical data science, which will contribute to robust immune subtype discovery and precision therapy insights.

Two representative publications from supervisors:

Y. Chen, S. Liu, L.G Papageorgiou, K. Theofilatos, S. Tsoka, “Optimisation Models for Pathway Activity Inference in Cancer”, Cancers, 15(6), 1787, 2023 (doi: 10.3390/cancers15061787)

Yahui Long, Kok Siong Ang, Mengwei Li, Kian Long Kelvin Chong, Raman Sethi, Chengwei Zhong, Hang Xu, Zhiwei Ong, Karishma Sachaphibulkij, Ao Chen, Zeng Li, Huazhu Fu, Min Wu, Lina Hsiu Kim Lim, Longqi Liu, Jinmiao Chen, “Spatially informed clustering, integration and deconvolution of spatial transcriptomics with GraphST”, Nature Communications, 14, 1155, 2023

5.1 Developing a computational model of the molecular permeation mechanisms of antibiotics through membranes of bacterial pathogens

Co-Supervisor 1A: Professor Martin Ulmschneider

Faculty: Faculty of Natural, Mathematical & Engineering Sciences

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Co-Supervisor 1B: Dr Peter J. Bond

Research Institute: Bioinformatics Institute (BII)

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Project Description:

Growing resistance of pathogenic bacterial strains against antibiotics is posing one of the largest global public health threats of our time. The cell envelope represents the main defensive barrier of bacteria against antibiotics. Nevertheless, the role of this barrier for antibiotic transport is not understood, chiefly due to a lack of experimental techniques that can capture the transport of drugs across the cell envelope at atomic resolution and in real time.

Here we will apply a combination of state-of-the-art computational approaches including unbiased atomic resolution simulations with sophisticated multiscale and AI analysis tools to capture the molecular mechanisms, transport rates, and energetics of antibiotic uptake by pathogenic bacteria. This project leverages the transformative growth in computational power and predictive accuracy of unbiased atomic detail molecular mechanics simulations to provide unprecedented insights that will allow designing of new antibiotics, as well as repurposing and retuning existing antibiotics that bacteria have become resistant against.

The project will provide cross-disciplinary doctoral training in both experimental and computational techniques, equipping the student with a broad skillset and techniques for molecular drug design. The first year's goal is to develop a molecular model of the bacterial membrane, that will form the basis for computational and experimental exploration of the transport process. Years 2 & 3 will probe this model with computational techniques to provide insights for experimental validation and tuning in year 4.

Working at both KCL and A*STAR will provide a vibrant cross-cultural and cross-disciplinary experience that will lay the foundation for closer collaborations.

Two representative publications from supervisors:

Chen CH, Starr CG, Troendle E, Wiedman G, Wimley WC, Ulmschneider JP, Ulmschneider MB. Simulation-Guided Rational de Novo Design of a Small Pore-Forming Antimicrobial Peptide. J Am Chem Soc. 2019 Mar 27;141(12):4839-4848.

Kaur H, Jakob RP, Marzinek JK, Green R, Imai Y, Bolla JR, Agustoni E, Robinson CV, Bond PJ, Lewis K, Maier T, Hiller S. The antibiotic darobactin mimics a β-strand to inhibit outer membrane insertase. Nature. 2021 May;593(7857):125-129.

THEME2: Neuroscience and Mental Health

1.2 Dissecting the cognitive and mental health in the Genetics Links to Anxiety and Depression and the HELIOS/SG100K cohort.

Co-Supervisor 1A: Professor Gerome Breen

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Co-Supervisor 1B: Professor Liu Jian Jun and Dr Max Lam

Research Institute: Genome Institute of Singapore / Institute of Mental Health

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Website: https://www.a-star.edu.sg/gis/our-people/faculty-staff/members/jian-jun-liu / https://www.researchgate.net/profile/Max-Lam

Project Description:

The project aims to investigate how genetics and the environment influence mental health and cognitive abilities, comparing findings between the UK and Singapore. Using two large datasets, the research will analyze genetic information along with mental and cognitive health assessments to understand the role of these factors in anxiety, depression, and cognitive function.

The GLAD Study and the HELIOS Study provide the data for this research. The GLAD Study has gathered information from about 58,000 individuals, including genome-wide genotyping on 35,000 and nanopore whole genome sequencing on >16000, and mental health assessments. The HELIOS Study in Singapore has recruited 70,000 participants with detailed health and cognitive data, and the first 10,000 have had their entire genome sequenced.

The project will use statistical methods to predict which cognitive factors correlate with mental health conditions and to identify genetic variations associated with these traits. It will also explore the impact of structural genetic variations on mental and cognitive health.

Findings will be disseminated through publications, presentations at meetings, and collaborations with charities, clinicians, industry, and policymakers. The goal is to facilitate the adoption of the research outcomes and address social and ethical issues related to genetic predictions of mental health.

Two representative publications from supervisors:

Davies MR, … NIHR BioResource consortium; Eley TC, Breen G. The Genetic Links to Anxiety and Depression (GLAD) Study: Online recruitment into the largest recontactable study of depression and anxiety. Behav Res Ther. 2019 Dec;123:103503. doi: 10.1016/j.brat.2019.103503. Epub 2019 Oct 24. PMID: 31715324; PMCID: PMC6891252.

Lam M, …. Deary IJ, Glahn DC, Malhotra AK, Lencz T. Pleiotropic Meta-Analysis of Cognition, Education, and Schizophrenia Differentiates Roles of Early Neurodevelopmental and Adult Synaptic Pathways. Am J Hum

Genet. 2019 Aug 1;105(2):334-350. doi: 10.1016/j.ajhg.2019.06.012. PMID: 31374203; PMCID: PMC6699140.

2.2 Understanding the role of socioeconomic disadvantage in neurodevelopment and the development of psychopathology during childhood and adolescence.

Co-Supervisor 1A: Professor Paola Dazzan and Dr Divyangana Rakesh

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Co-Supervisor 1B: Dr Evelyn Law and Professor Michael Meaney

Research Institute: Singapore Institute of Clinical Sciences (SICS)

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Project Description:

Our research project explores how early-life-environments can influence both brain development and mental health in young people. In particular, the neighbourhood children grow up in plays a crucial role in children's mental health and well-being. However, while prior studies have correlated neighborhood-level disadvantage with changes in brain function, the precise neurobiological roots of this link with mental health remain unclear. Our project seeks to address these knowledge gaps. First, we will test if changes in brain function mediate associations between growing up in a disadvantaged neighbourhood and mental health problems both during early childhood and adolescence using rich longitudinal data. Second, considering the multifaceted nature of neighbourhood disadvantage, the project aims to identify specific factors—such as access to green spaces, pollution levels, noise, and crime rates—that may exert the most pronounced effects on both brain development and mental health.

We will use data from two major studies: the Adolescent Brain Cognitive Development (ABCD) Study, tracking 11,500 children aged 9-10, and the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) study, monitoring 1,176 children born 2009-2011 and currently aged 14. The PhD student will gain skills in theoretical conceptualization, MRI analysis, programming, and statistical methods such as linear mixed models and structural equation modeling. By improving our understanding of these connections, we aim to enhance support for young people's mental health. If you're interested in exploring these crucial questions and developing skills in neuroscience, psychology, and public health, consider joining our project.

Two representative publications from supervisors:

Ma X, Biaggi A, Sacchi C, Lawrence AJ, Chen PJ, Pollard R, Matter M, Mackes N, Hazelgrove K, Morgan C, Harding S, Simonelli A, Schumann G, Pariante CM, Mehta M, Montana G, Rodriguez-Mateos A, Nosarti C, Dazzan P. Mediators and moderators in the relationship between maternal childhood adversity and children's emotional and behavioural development: a systematic review and meta-analysis. Psychol Med. 2022 Jul;52(10):1817-1837. doi: 10.1017/S0033291722001775. Epub 2022 Jun 22. PMID: 35730541; PMCID: PMC9340854.

Rakesh, D., Whittle, S., Sheridan, M. A., & McLaughlin, K. A. (2023). Childhood socioeconomic status and the pace of structural neurodevelopment: accelerated, delayed, or simply different? Trends in Cognitive Sciences.

THEME3: Biomedical Engineering and Medical Imaging

1.3 Design, Modelling, and Implementation of Hybrid Continuum Multi-Arm Robots

Co-Supervisor 1A: Professor Christos Bergeles

Faculty: Faculty of Life Sciences & Medicine

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Co-Supervisor 1B: Wang Yuzhe and Teo Chek Sing

Research Institute: Singapore Institute of Manufacturing Technology (SIMTech)

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Website: https://www.a-star.edu.sg/simtech/

Project Description:

Continuum robots are snake-like robotic systems that can change their shape and control the position and orientation of their tip. By changing their shape, they can conform to the anatomy, making them appropriate for deployment within human lumen, or in sensitive areas such as the brain. Predominantly, continuum robots are single-arm robots, which means the operate more akin to a steerable needle. However, to carry out surgery and intervention, for example for tumour excision, these robots need to be modified to allow for bimanual manipulation of tissue, and the inclusion of an endoscope to visualise the area of the pathology. Adding more arms implies that new robot architectures need to be investigated, while new understanding of the interplay between the various flexible structures should also be developed. This PhD research project will investigate this new type of robotic systems, and come up with novel designs, models, and way to control them to achieve enhanced surgical precision in confined spaces.

Two representative publications from supervisors:

Bergeles, Christos, et al. "Concentric tube robot design and optimization based on task and anatomical constraints." IEEE Transactions on Robotics 31.1 (2015): 67-84.

Wang, Yuzhe, et al. "Insect-scale jumping robots enabled by a dynamic buckling cascade" Proceedings of the National Academy of Sciences 120 (5), e2210651120, 2023.

2.3 Tactile-aided Visual Navigation and Localisation for Robot-assisted Minimally Invasive Surgeries

Co-Supervisor 1A: Dr Shan Luo

Faculty: Faculty of Natural, Mathematical & Engineering Sciences

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Co-Supervisor 1B: Dr Yan Wu

Research Institute: Institute for Infocomm Research

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Website: https://research.a-star.edu.sg/researcher/yan-wu/

Project Description:

The research project aims to transform minimally invasive surgery, making it safer and more precise. A system that combines the sense of touch with advanced computer vision will be developed, enhancing the accuracy of surgical instruments and enabling the identification of tissue properties during surgery. By integrating tactile sensors, surgical cameras, and CT scans, we can create a comprehensive map of the surgical environment. This map will help surgeons navigate and locate instruments more accurately, reducing the risk of complications and improving patient care.

Throughout the project, the student will gain a highly interdisciplinary set of skills (mathematics, statistics, computation, data analytics and informatics, machine learning and Artificial Intelligence, imaging and engineering) and practical experience in cutting-edge fields like computer vision and robotics. They will become proficient in deep learning libraries like PyTorch and TensorFlow, crucial for the future of medical technology. Working with novel sensing technologies, including tactile sensors, will allow the student to develop expertise in multimodal data integration for enhanced surgical procedures.

The objectives for each year are (1) comprehensive literature review, integration of tactile sensors, surgical cameras and CT scans, and early data collection. (2) gathering extensive data, and data analysis for projecting tactile tissue property to visual maps. (3) experiment validation and embedding improved localisation in tumour removal. (4) pre-clinical validation, further optimization, addressing limitations, and ensuring system scalability.

Two representative publications from supervisors:

Dr Shan Luo: Lee, J.T., Bollegala, D. and Luo, S., 2019. “Touching to See” and “Seeing to Feel”: Robotic Cross-modal Sensory Data Generation for Visual-Tactile Perception. In 2019 International Conference on Robotics and Automation (ICRA) (pp. 4276-4282). IEEE.

Dr Yan Wu: Li. Y., Tee K.P., Yan R., Chan W.L., Wu Y,. A framework of human–robot coordination based on game theory and policy iteration. IEEE Transactions on Robotics (2016).

3.3 Rapid multi-frequency MR Elastography for the assessment of liver fibrosis and inflammation in non-alcoholic fatty liver disease

Co-Supervisor 1A: Dr Radhouene Neji

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Co-Supervisor 1B: Dr Sarah Luo and Dr Fu Yu

Research Institute: Institute of Molecular and Cell Biology (IMCB)

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Website: https://www.a-star.edu.sg/imcb/imcb-research/scientific-programmes/neurometabolism-in-health-diseases/sarah-luo /

https://www.a-star.edu.sg/imcb/imcb-research/scientific-programmes/neurometabolism-in-health-diseases/fu-yu

Project Description:

Non-alcoholic fatty liver disease (NAFLD) is a global health crisis, affecting around around 25% of the world population and its prevalence rate is expected to increase. NAFLD may lead to liver damage, liver failure and liver cancer. It is therefore of high importance to enable early diagnosis and risk stratification in NAFLD for an improved patient management. The goal of this PhD project is to develop a rapid MRI technique to enable simultaneous assessment of liver fibrosis and inflammation in NAFLD based on MR Elastography, and to validate this technique in a pre-clinical animal model and in a cohort of NAFLD patients. This will involve the development of novel MRI acquisition, data reconstruction and post-processing techniques. The student will benefit from expertise at KCL (MRI physics, MR pulse sequence development) and A*STAR (preclinical imaging and biology) and will have the opportunity to be trained in MR pulse sequence development and MRI reconstruction by the MR staff scientists of Siemens Healthineers working together with the KCL researchers on-site. The student will also have the opportunity to collaborate with the National Institutes of Health (NIH), Bethesda, MA, USA on the clinical translation of the techniques they develop.

Two representative publications from supervisors:

Darwish OI, Gharib AM, Jeljeli S, Metwalli NS, Feeley J, Rotman Y, Brown RJ, Ouwerkerk R, Kleiner DE, Stäb D, Speier P, Sinkus R, Neji R. Single Breath-Hold 3-Dimensional Magnetic Resonance Elastography Depicts Liver Fibrosis and Inflammation in Obese Patients. Invest Radiol. 2023 Jun 1;58(6):413-419.

Luo SX, Huang J, Li Q, Mohammad H, Lee CY, Krishna K, Kok AM, Tan YL, Lim JY, Li H, Yeow LY, Sun J, He M, Granjean J, Sajikuma S, Han W, Fu Y. Regulation of feeding by somatostatin neurons in the tuberal nucleus. Science. 2018 Jul 6;361; 76-81