

A*STAR and King's College London PhD Studentships October 2025 Entry

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A*STAR and King's College London PhD Studentships

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:

- 1. Cells, Molecules and the Basis of Health and Disease: THEME1_2025
- 2. Neuroscience and Mental Health: THEME2_2025
- 3. Biomedical Engineering and Medical Imaging: THEME3_2025

Important dates:

Application Stage	Date
Deadline for application	Sunday, 23 February 2025, 23:59 UK Time
Application Outcome	By 28 March 2025
Interviews	Week commencing 07 April 2025
Interview Outcomes	By 11 April 2025
Acceptance of studentship offer	By 25 April 2025
Degree Start Date	October 2025

The 2025/26 studentships will commence in October 2025. For further information or queries relating to the application process, please contact: <u>doctoralstudies@kcl.ac.uk</u>.

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 Molecular basis of treatment response in glioblastoma multiforme using nanoneedle-based spatio-temporal transcriptomics

Co-Supervisor King's (1): Dr Ciro Chiappini Faculty: Faculty of Dentistry, Oral & Craniofacial Sciences E-mail: <u>ciro.chiappini@kcl.ac.uk</u> Website: <u>https://chiappinilab.com</u>

Co-Supervisor A*STAR (1): Dr Chen Kok Hao Research Institute: Genome Institute of Singapore Email: <u>chenkh@gis.a-star.edu.sg</u> Website: <u>https://khchenlab.github.io</u>

Co-Supervisor A*STAR (2): Dr Shyam Prabhakar Research Institute: Genome Institute of Singapore

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Website: https://www.a-star.edu.sg/gis/our-people/faculty-staff/members/shyam-prabhakar

Project Description:

Glioblastoma multiforme (GBM) is a dilapidating disease with very poor prognosis. The average survival time is ~1 year even with treatment. Researchers are actively working on understanding the disease to come up with new treatment that can improve the outcomes. GBM is a type of brain cancer that grows aggressively and arises from the brain supportive tissue called glial cells. But many different types of cells are involved, including immune cells, neuronal cells, and endothelial cells. The molecular changes underlying tumorigenesis and therapeutic response occur in these cells over several days or weeks and are not well understood. The aim of this project is to develop a novel nanotechnology enabled device that can non-destructively study the molecular and cellular response to tissue injuries in cells and living animals. By charting the tumorigenesis and therapeutic response process over time, we hope to uncover genes that are important that will enable us to search for more durable and effective therapeutics.

One representative publication from supervisors:

Martella, D. A. et al. Nondestructive Spatial Lipidomics for Glioma Classification. bioRxiv 2023.03.09.531882 (2023) doi:10.1101/2023.03.09.531882.

Chen, K. H., Boettiger, A. N., Moffitt, J. R., Wang, S. & Zhuang, X. Spatially resolved, highly multiplexed RNA profiling in single cells. Science. 348, science.aaa6090- (2015).

Singhal et al. BANKSY unifies cell typing and tissue domain segmentation for scalable spatial omics data analysis. https://doi.org/10.1038/s41588-024-01664-3.

2.1 Investigating the importance of tryptophan metabolism in pregnancy and its consequences for offspring health

Co-Supervisor King's (1): Dr Kim Jonas Faculty: Faculty of Life Sciences & Medicine E-mail: <u>kim.jonas@kcl.ac.uk</u> Website: <u>https://www.kcl.ac.uk/people/kim-jonas</u>

Co-Supervisor King's (2): Dr Norah Fogarty

Faculty: Faculty of Life Sciences & Medicine

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Website: https://www.kcl.ac.uk/research/trophoblast-and-human-embryo-lab

Co-Supervisor A*STAR (1): Dr Hannah Yong

Research Institute: Institute for Human Development and Potential

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Website: <u>https://www.a-star.edu.sg/ihdp/our-science/research-programmes/human-development-researchers</u>

Co-Supervisor A*STAR (2): A/Prof Shiao-Yng Chan

Research Institute: Institute for Human Development and Potential

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Website: https://medicine.nus.edu.sg/obgyn/research/our-researchers/Chan-Shiao-yng.html

Project Description:

The correct functioning of the placenta at all stages of development is critical for a healthy pregnancy and lifelong health. Tryptophan is an essential nutrient found in the diet and is necessary for healthy growth and development *in utero*. This project will investigate the role of tryptophan metabolism in regulating placental function and examine the consequence of aberrant metabolism on pregnancy and long-term offspring health outcomes. The successful applicant will be trained in the areas of developmental/reproductive biology and intrauterine programming of long-term health. The first 2 years will be spent at the Centre for Gene Therapy and Regenerative Medicine and the Department of Women and Children's Health at King's College London to determine the role of tryptophan in placental function and the downstream regulatory mechanisms involved using *in vitro* and *ex vivo* models of human placenta and molecular biology techniques including RT-qPCR, immunofluorescence and super-resolution imaging and cellular phenotyping assays. The student will gain expertise in stem cell culture and manipulation as well as standard molecular biology techniques.

Training in microscopy will be provide by the supervisors as well as the Nikon Imaging Centre, KCL. Bioinformatics training can be provided by the Hub for Applied Bioinformatics. The latter 2 years will be spent at A*STAR Institute for Human Development and Potential, where the consequences of aberrant tryptophan metabolism on pregnancy and offspring health outcomes will be explored with biostatistics and bioinformatic approaches using longitudinal data from the Singapore GUSTO mother-child cohort.

One representative publication from supervisors:

Balestrini PA, Abdelbaki A, McCarthy A, Devito L, Senner CE, Chen AE, Munusamy P, Blakeley P, Elder K, Snell P, Christie L, Serhal P, Odia RA, Sangrithi M, Niakan KK, <u>Fogarty NME</u>. *Transcription factor-based transdifferentiation of human embryonic to trophoblast stem cells*. Development. 2024;151(17):dev202778.

Agwuegbo UT, Colley E, Albert AP, Butnev VY, Bousfield GR, Jonas KC. Differential FSH Glycosylation Modulates FSHR Oligomerization and Subsequent cAMP Signaling. Front Endocrinol (Lausanne). 2021 Dec 3;12:765727. doi: 10.3389/fendo.2021.765727. PMID: 34925235; PMCID: PMC8678890.

Fitzgerald E, Shen MJ, <u>Yong HEJ</u>, Wang Z, Pokhvisneva I, Patel S, O'Toole N, Chan SY, Chong YS, Chen H, Gluckman PD, Chan J, Lee PKM, Meaney MJ. *Hofbauer cell function in the term placenta associates with adult cardiovascular and depressive outcomes*. Nature Communications 2023;14(1):7120.

Chu AHY, Tint MT, Chang HF, Wong G, Yuan WL, Tull D, Nijagal B, Narayana VK, Meikle PJ, Chang KTE, Lewis RM, Chi C, Yap FKP, Tan KH, Shek LP, Chong YS, Gluckman PD, Lee YS, Fortier MV, Godfrey KM, Eriksson JG, Karnani N, <u>Chan SY</u>. High placental inositol content associated with suppressed pro-adipogenic effects of maternal glycaemia in offspring: the GUSTO cohort. Int J Obes (Lond). 2021;45(1):247-257.

3.1 Characterisation of nuclear envelope proteins in skin across the human lifespan and their role in modulating fibrosis in cardiac and skin fibroblasts

Co-Supervisor 1A: Dr Matthew Stroud Faculty: Faculty of Life Sciences & Medicine E-mail: <u>matthew.stroud@kcl.ac.uk</u> Website: <u>STROUD LAB - Home</u>

Co-Supervisor A*STAR (1): Yin Loon Lee Research Institute: A*STAR Skin Research Labs Email: <u>yinloon_lee@asrl.a-star.edu.sg</u> Website: <u>https://scholar.google.com/citations?user=H7FFwbcAAAAJ&hl=en</u>

Co-Supervisor A*STAR (2): Leah Vardy Research Institute: A*STAR Skin Research Labs Email: <u>leah_vardy@asrl.a-star.edu.sg</u> Website: <u>https://www.a-star.edu.sg/asrl/principal-investigators/leah-vardy</u>

Project Description:

The extracellular matrix (ECM) forms a network of fibres between cells in solid organs. Modulation of ECM deposition is essential both for proper heart development, but also after harmful insults such as a heart attack. Elevated ECM deposition in the heart can result in excessive scarring that is detrimental for normal function, such as during ageing, or after a heart attack. In contrast, loss of ECM production is associated with skin aging. Signalling pathways are known to regulate ECM deposition but many details remain unclear, in particular, the role of the nuclear envelope. The nuclear envelope sits at the interface between the genome and the cell skeleton. One group of proteins lining the nuclear envelope and interacting with the force-transmitting cell skeleton are the Linker of Nucleoskeleton and Cytoskeleton complexes. The LEM domain class of nuclear envelope proteins regulate signalling pathways that determine scar formation or fibrosis in tissue, though the precise details of how this occurs is unclear. The overarching goals of this PhD are to uncover the mechanisms by which the nuclear envelope modulates fibrosis in cells and tissue systems.

Year 1: Screenings to identify nuclear envelope factors that regulate scarring in both heart and skin.

Year 2/3: Validation of screening hits and protein-protein interactions in cells

Year 3/4: Cell biology and in vivo validation of putative protein interactors and screening hits. Thesis writing (3m).

One representative publication from supervisors:

Ross JA...**Stroud MJ**^{\$}. Lem2 is essential for cardiac development by maintaining nuclear integrity. *Cardiovasc Res.* 2023. <u>doi: 10.1093/cvr/cvad061.</u>

Leong EL... **Lee YL**. Nesprin-1 LINC complexes recruit microtubule cytoskeleton proteins and drive pathology in *Lmna*-mutant striated muscle. *Hum Mol Genet*. 2023 Jan 6;32(2):177-191. doi: 10.1093/hmg/ddac179.

Lim HK, Rahim AB, Leo VI, Das S, Lim TC, Uemura T, Igarashi K, Common J, **Vardy LA**. Polyamine Regulator AMD1 Promotes Cell Migration in Epidermal Wound Healing. J Invest Dermatol. 2018 Dec;138(12):2653-2665. doi: 10.1016/j.jid.2018.05.029. Epub 2018 Jun 12. PMID: 29906410.

4.1 Comparative Analysis of Bacterial Determinants Contributing to Persistent Infections in the Zebrafish Model

Co-Supervisor 1A: Dr Vincenzo Torraca Faculty: Faculty of Life Sciences & Medicine E-mail: <u>vincenzo.torraca@kcl.ac.uk</u> Website: <u>https://www.kcl.ac.uk/people/vincenzo-torraca</u>

Co-Supervisor 1B: Dr Stefan Oehlers Research Institute: A*STAR Infectious Diseases Labs Email: <u>anand_andiappan@immunol.a-star.edu.sg</u> Website: <u>https://www.a-star.edu.sg/idlabs/about-us/people/our-investigators/stefan-oehlers</u>

Project Description:

This PhD project explores how certain bacteria evade the immune system and establish longlasting infections. The project will focus on two prototypical bacteria that are known to establish persistent infections: Shigella sonnei, an important diarrhoeal pathogen, and Mycobacterium marinum, a close relative of the bacterium that causes tuberculosis. The project will take advantage of the zebrafish as a model organism, which allows to directly observe infection and immune responses, thanks to the transparency in early life stages. The project will provide the student with training in advanced molecular biology and microbiology techniques, including live imaging, gene editing (i.e., CRISPR/Cas9), bacterial genetics, and bioinformatics for data analysis. This training will equip the student with a wide-ranging skill set applicable across infection biology and immunology research.

Our overarching objective is to reveal how bacteria persist within the host and evade immune defences, especially focusing on the role of certain immune cells (i.e., macrophages) as potential hiding spots for persistent bacteria and certain immune signalling molecules (i.e., interferons) as potential systems to control persistent infections. The findings from this research may guide the development of better treatments for persistent bacterial infections that do not respond to traditional therapies, benefiting public health. This project offers a unique opportunity for a PhD candidate to work internationally and gain diverse research experience.

One representative publication from supervisors:

Torraca V*, Brokatzky D, Miles SL, Chong CE, De Silva PM, Baker S, Jenkins C, Holt KE, Baker KS, Mostowy S. Shigella serotypes associated with carriage in humans establish persistent infection in zebrafish. J Infect Dis. 2023 Oct 18;228(8):1108-1118. DOI: 10.1093/infdis/jiad326. *Co-corresponding author.

Kam JY, Hortle E, Krogman E, Warner SE, Wright K, Luo K, Cheng T, Manuneedhi Cholan P, Kikuchi K, Triccas JA, Britton WJ, Johansen MD, Kremer L, Oehlers SH*. Rough and smooth variants of Mycobacterium abscessus are differentially controlled by host immunity during chronic infection of adult zebrafish. Nat Commun. 2022 Feb 17;13(1):952. DOI: 10.1038/s41467-022-28638-5. *Corresponding author.

THEME2: Neuroscience and Mental Health

1.2 Unraveling the Epigenetic Links Between Maternal Health, Physical Activity, and Neurodevelopmental Outcomes in Children

Co-Supervisor 1A: Dr Chloe Wong Faculty: Institute of Psychiatry, Psychology & Neuroscience E-mail: <u>chloe.wong@kcl.ac.uk</u> Website: <u>https://www.kcl.ac.uk/people/chloe-wong</u>

Co-Supervisor 1B: Professor Alina Rodriguez

Research Institute: Institute for Human Development and Potential

Email: <u>alina_rodriguez@sics.a-star.edu.sg</u>

Website: <u>https://www.a-star.edu.sg/ihdp/our-science/research-programmes/human-development-researchers</u>

Project Description:

This research project investigates how maternal health and lifestyle, specifically obesity and physical activity, could influence children's neurodevelopment. Neurodevelopmental conditions such as attention difficulties, learning challenges, and social-emotional difficulties are influenced by complex interactions between genetic and environmental factors. By focusing on epigenetics, the study aims to uncover biological markers that bridge the gap between maternal health and children's developmental trajectories.

Leveraging the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort, a globally unique dataset, the project will explore how maternal health factors shape epigenetic patterns in children. These patterns could influence outcomes such as cognitive function, emotional regulation, and social interaction from infancy through adolescence.

This PhD program provides comprehensive training in cutting-edge research methodologies, including epigenetic analysis, neurodevelopmental assessments, and advanced statistical modeling. The student will spend split time at King's College London (London, UK) and A*STAR (Singapore) and gain invaluable experience in international collaboration, data integration, and public science communication.

Yearly Objectives:

- **Year 1**: Build a strong foundation by preparing data, conducting a literature review, and starting training in advanced epigenetic analysis techniques.
- Year 2: Investigate links between maternal health and epigenetic signatures, and analyse child neurodevelopmental trajectories.
- Year 3: Focus on predictive modeling and publish preliminary findings in peer-reviewed journals.
- **Year 4**: Finalize predictive models, write the PhD thesis, and present findings at conferences and public workshops.

This research holds the potential to identify actionable insights into modifiable risk factors, paving the way for early interventions and personalised strategies to support healthy neurodevelopment in children.

One representative publication from supervisors:

Alameda, L., Trotta, G., Quigley, H., Rodriguez, V., Gadelrab, R., Dwir, D., Dempster, E., Wong, C. C. Y., & Di Forti, M. (2022). Can epigenetics shine a light on the biological pathways underlying major mental disorders? Psychological Medicine, 52, 1645-1665. <u>https://doi.org/10.1017/S0033291721005559</u>.

Karhunen V, Bond TA, Zuber V, Hurtig T, Moilanen I, Järvelin MR, Evangelou M, Rodriguez A. The link between attention deficit hyperactivity disorder (ADHD) symptoms and obesityrelated traits: genetic and prenatal explanations. Transl Psychiatry. 2021 Sep 4;11(1):455. doi: 10.1038/s41398-021-01584-4. https://pubmed.ncbi.nlm.nih.gov/34482360/.

2.2 Integrating neuroimaging and omics to unravel the link between early life stress and depression in children and adolescents

Co-Supervisor King's: Professor Paola Dazzan Faculty: Institute of Psychiatry, Psychology & Neuroscience E-mail: <u>paola.dazzan@kcl.ac.uk</u> Website: <u>https://www.kcl.ac.uk/people/paola-dazzan</u>

Co-Supervisor A*STAR (1): Dr Ai Peng Tan

Research Institute: Institute for Human Development and Potential (IHDP)

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Website: <u>https://www.a-star.edu.sg/ihdp/our-science/research-programmes/translational-neuroscience-researchers</u>

Co-Supervisor A*STAR (2): Professor Michael Meaney

Research Institute: Singapore Institute of Clinical Sciences (SICS)

Email: <u>michael_meaney@sics.a-star.edu.sg</u>

Website: https://research.a-star.edu.sg/researcher/michael-meaney

Project Description:

Psychiatric disorders are described as the 'chronic disease of the young', with a peak onset at age 14–15 years. It is therefore critical to elucidate what factors, in the biology of the body, lead to the development of these disorders.

Early life stress (ELS) in particular is associated with the onset of depression in childhood and adolescence. However, we do not know whether this stress is also associated with changes in how the brain develops in young people. Furthermore, we do not know whether other changes, like those that happen when the body responds to stress (for example with low level inflammation) or someone's genetic makeup also affect how the brain develops, and the risk of developing depression. To fill these gaps, this project will integrate measures of brain development (that give information on volumes, function and chemical composition like diffusion imaging, resting-state fMRI, and MR spectroscopy), activation of the immune response (i.e serum CRP, cytokines, hair and salivary cortisol, urinary polyphenols), epigenetic (DNAm) and genetic (PRS scores) profiles from multiple existing datasets to develop a predictive model of depression.

The selected PhD student will be offered the opportunity to work with highly interdisciplinary and collaborative teams across KCL and A*STAR IHDP and acquire critical skills in the following areas: advanced multimodal neuroimaging techniques, integrative omics, clinical developmental psychiatry, state-of-the-art statistical methods, and machine learning approaches. These will be compleme

One representative publication from supervisors:

Pollard R, Chen PJ, Mackes N, Lawrence AJ, Ma X, Matter M, Kretzer S, Morgan C, Harding S, Schumann G, Pariante C, Mehta M, Montana G, Nosarti C, Desrivieres S, Rodriguez-Mateos A, Dazzan P. The eBRAIN study: The impact of early adversity on trajectories of brain maturation and mental health in young adolescents - A prospective cohort study. Brain Behav Immun Health. 2022 Oct 28;26:100539. doi: 10.1016/j.bbih.2022.100539. PMID: 36388138; PMCID: PMC9640307.

A Glucocorticoid-Sensitive Hippocampal Gene Network Moderates the Impact of Early-Life Adversity on Mental Health Outcomes. Arcego DM, Buschdorf JP, O'Toole N, Wang Z, Barth B, Pokhvisneva I, Rayan NA, Patel S, de Mendonça Filho EJ, Lee P, Tan J, Koh MX, Sim CM, Parent C, de Lima RMS, Clappison A, O'Donnell KJ, Dalmaz C, Arloth J, Provençal N, Binder EB, Diorio J, Silveira PP, Meaney MJ. Biol Psychiatry. 2024 Jan 1;95(1):48-61. doi: 10.1016/j.biopsych.2023.06.028. Epub 2023 Jul 3. PMID: 37406925.

THEME3: Biomedical Engineering and Medical Imaging

1.3 Engineered Exosomes for Targeted Treatment of Hypertrophic Heart Failure

Co-Supervisor 1A: Dr Driton Vllasaliu Faculty: Faculty of Life Sciences & Medicine E-mail: <u>driton.vllasaliu@kcl.ac.uk</u> Website: <u>https://www.kcl.ac.uk/people/driton-vllasaliu</u>

Co-Supervisor 1B: Dr Boon Seng Soh

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

Email: <u>bssoh@imcb.a-star.edu.sg</u>

Website: https://research.a-star.edu.sg/researcher/soh-boon-seng/

Project Description:

The onset of heart failure, which affects over 64 million people worldwide, is typically preceded by cardiac hypertrophy. Current treatments for hypertrophic heart failure are inadequate and there is a major need for more effective therapeutic options.

Exosomes are microscopic fat bubbles (around 1,000 times smaller than the diameter of a human hair) produced by cells, which play a key role in cell-cell communication by transferring biologically active substances. Certain exosomes, such as those from mesenchymal stem cells (MSC; cells which generate all other specialist cells of the body) have been shown to have therapeutic potential in cardiac hypertrophy. In this project, we will engineer stem cell exosomes to drastically enhance their therapeutic potential. This will be achieved by 1) manipulating their cargo molecules, introducing specific molecules shown to attenuate cardiac hypertrophy, and 2) enabling targeted delivery of these engineered exosomes to the heart. We expect these engineered exosomes to demonstrate very strong therapeutic activity with the potential to be the next generation of therapies for cardiac hypertrophy and heart failure.

<u>Skills:</u>

The project will provide the student with state-of-the-art skills in exosomes, stem cells, organoid models and RNA therapies.

Over-arching objectives for each year:

Year 1: To isolate, characterise and determine the baseline anti-hypertrophic effects of naïve MSC exosomes. Year 2: To generate RNA-loaded engineered MSC exosomes and screen therapeutic activity in organoid model.

Year 3: To generate RNA-loaded and targeted engineered MSCs and demonstrate proof of efficacy and targeting in organoid model.

Year 4: Publications and thesis.

One representative publication from supervisors:

Zhang et al. Probing milk extracellular vesicles for intestinal delivery of RNA therapies. J Nanobiotechnology 2023, 21(1):406, DOI: 10.1186/s12951-023-02173-x.

Ho et.al. Robust generation of human-chambered cardiac organoids from pluripotent stem cells for improved modelling of cardiovascular diseases. Stem Cell Res Ther. 2022 Dec 21;13(1):529. DOI:10.1186/s13287-022-03215-1.

2.3 Tailored grasping assistance for individuals with motor impairments via learning in simulation

Co-Supervisor 1A: Dr Letizia Gionfrida Faculty: Faculty of Natural, Mathematical & Engineering Sciences E-mail: <u>letizia.gionfrida@kcl.ac.uk</u> Website: <u>https://www.kcl.ac.uk/people/letizia-gionfrida</u>

Co-Supervisor 1B: Dr Haiyue Zhu Research Institute: Singapore Institute of Manufacturing Technology (SIMTech) Email: <u>zhu_haiyue@simtech.a-star.edu.sg</u> Website: <u>https://research.a-star.edu.sg/researcher/haiyue-zhu/</u>

Project Description:

Neurological conditions such as stroke often lead to difficulties with hand movement, making it hard for people to perform everyday tasks. This project aims to develop a personalized robotic glove that can help individuals regain hand function and improve their independence.

The robotic glove will adapt to each person's unique needs using cutting-edge technologies. First, we will analyze videos of healthy hand movements to understand how hands naturally move during tasks like picking up objects. Then, we will use computer simulations to recreate hand impairments caused by muscle weakness, allowing us to test and improve the glove's ability to provide support. Finally, we will design a smart control system for the glove, so it works seamlessly with the user's hand to assist with tasks.

The student will receive training in advanced robotics, artificial intelligence, and biomedical engineering. By the end of the project, the research will provide a customizable, effective, and affordable rehabilitation solution for people with hand impairments, potentially transforming their quality of life.

One representative publication from supervisors:

Letizia Gionfrida: https://www.science.org/doi/10.1126/scirobotics.adj8812.

Haiyue Zhu: https://ieeexplore.ieee.org/abstract/document/10612766.