List of Research Projects Available for Prospective PhD Students at LKCMedicine

The list of research projects is grouped by the following 9 Research Areas.

1. Neuroscience & Mental Health
2. Nutrition, Metabolism & Health
3. Population & Global Health
4. Respiratory & Infectious Diseases
5. Skin Disease & Wound Repair
6. Data Science & Artificial Intelligence
7. Cancer Discovery & Regenerative Medicine
8. Microbiome Medicine
9. Medical Education
10. Others

Funding Opportunities:

Some research projects may offer potential funding or scholarship support. Where applicable, remarks will be indicated under the ***Project Title***. Prospective candidates are strongly encouraged to contact the respective project main supervisor directly to discuss project scope, funding availability and specific application deadlines for scholarships or funding.

No	Project Title with Brief Description	Principal Investigator
	1. Neuroscience & Mental Health	
1.1	**Brain mechanisms for executive function and their vulnerability to ageing, stress, and psychosis** The project aims to elucidate the brain-wide mechanisms underpinning executive functions and their deterioration due to ageing, stress, and psychosis using behaving mice as a model system. The student will address this problem utilizing cutting-edge neuroscience technologies, including in-vivo calcium imaging, optogenetics, and the development of behavioral paradigms. Additionally, the student will receive extensive training in coding and data analysis. References: Chong HR., Ranjbar-Slamloo Y., Ho MZH., Ouyang X., and Kamigaki T.(2023) Functional alterations of the prefrontal circuit underlying cognitive aging in	**Asst Prof Tsukasa Kamigaki** tsukasar@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp01272

<table>
<tr>
<td>1.2</td>
<td>
mice. Nature Communications,14, 7254.

Kamigaki T., and Dan Y. (2017). Delay Activity of Specific Prefrontal Interneuron Subtypes Modulates Memory-Guided Behavior. Nature Neuroscience, 20, 854-863.

Understanding Mechanisms of Cellular Cholesterol Distribution: Implications for Brain Health

Neurodegeneration and age-associated decline in cognitive function are often associated with altered compositions of lipids (or “fats”) in the brain. Lipids play very important roles in regulating brain function, and abnormal distribution of lipids in neurons results in numerous neurological disorders. Among various lipids, cholesterol serves as a major building block for cellular membranes and maintains healthy neurons. In this project, we will use various cutting-edge techniques, including advanced microscopy, stem cells, and animal models, including *C. elegans*, to identify key molecular machineries that are responsible for the distribution of cellular cholesterol. As cholesterol metabolism plays an important role in brain health and animal physiology, our research has the potential to reveal new therapeutic targets for guiding major drug discovery efforts toward treating devastating neurodegenerative disorders, such as Alzheimer’s disease.

Selected References:

(1) Naito T, Ercan B, Krshnan L, Triebl A, Koh DHZ, Wei FY, Tomizawa K, Torta FT, Wenk MR, and Saheki Y (2019). Movement of accessible plasma membrane cholesterol by the GRAMD1 lipid transfer protein complex. ***eLife***. 8: e51401.
(2) Ercan B*, Naito T*, Koh DHZ, Dharmawan D, and Saheki Y (2021). Molecular basis of accessible plasma membrane cholesterol recognition by the GRAM domain of GRAMD1b. ***EMBO J***. 40: e106524. *Co-first authors.
(3) Naito T and Saheki Y (2021). GRAMD1-
</td>
<td>
Assoc Prof Yasunori Saheki

yasunori.saheki@ntu.edu.sg

Website

www.thesahekilab.com
</td>
</tr>
</table>

	mediated accessible cholesterol sensing and transport. ***BBA - Molecular and Cell Biology of Lipids***. 1866: 158957. (4) Naito T, Yang H, Koh DHZ, Mahajan D, Lu L, and Saheki Y (2023). Regulation of cellular cholesterol distribution via non-vesicular lipid transport at ER-Golgi contact sites. ***Nature Communications***. 14: 5867. (5) Koh DHZ, Naito T, Na M, Yeap YJ, Rozario P, Zhong FL, Lim KL, and Saheki Y (2023). Visualization of accessible cholesterol using a GRAM domain-based biosensor. ***Nature Communications***. 14: 6773.	
1.3	**Gut-brain neurobiology: microbiome control of neural circuits and behaviour** The trillions of bacteria living in our body encode over 46 million genes – suggesting tremendous functional capacity (by contrast, the human genome has less than a thousandth of that). Moreover, emerging evidence suggests that the gut microbiota profoundly influences host physiology and behaviour. In this project, we will investigate the fundamental biological basis of "gut-feelings", how microorganisms and chemicals in the gut signal to brain to modulate neural substrates that control physiology and behaviour. We employ a range of experimental techniques in mice to study the mammalian gut-brain axis including sequencing, metabolomics, in vivo neural imaging/recording, and genetically-guided functional interrogation.	**Asst Prof Hwei-Ee TAN** hweiee.tan@ntu.edu.sg 
1.4	**Structural and Functional Study of Extracellular Vesicles in Aging-related Neurodegeneration** Aging-related neurodegeneration, including Alzheimer's Disease and Parkinson's Disease, is a growing global health challenge, especially in aging societies like Singapore. Extracellular vesicles (EVs) are emerging as key players in neurodegeneration,	**Dr Chuchu Wang** choicewang0820@hotmail.com **Website** https://scholar.google.com/citations?user=1SQy-gQAAAAJ&hl=en&oi=ao

	potentially mediating disease propagation through altered lipid composition and transport of toxic proteins. This project aims to investigate how different ApoE isoforms, particularly the risk-associated ApoE4 and protective ApoE2, influence lipid regulation in EVs across aging. We will apply mass spectrometry-based lipidomics and cryo-electron microscopy to characterize EV lipid profiles and protein structures. The findings may uncover novel biomarkers for early dementia diagnosis and guide lipid-targeted therapeutic strategies to improve brain health in aging populations.	
1.5	**Bat-inspired targets to fight human diseases and aging** The objective is to learn from bats with exceptional disease resistance and healthy longevity, aiming to translate these lessons into new targets to fight human diseases and extend healthspan. The pioneering work in bat inflammation (*Nat Micro* 2019, *PNAS* 2020, *Nature* 2021, *Cell* 2023 and ongoing development of a new class of anti-inflammatory drugs) has helped establish bats as a great model to uncover new strategies to fight human diseases and has just scratched the surface of what we can learn from bats to benefit humans. The three different and synergistic approaches include 1) 'unbiased' multi-omics aging atlas of bats 2) 'disease centric' disease-free bat models including metabolic and neurological diseases and 3) 'more targeted' study of enhanced proliferation/regeneration and increased apoptosis as potential anti-aging/cancer mechanisms.	**Asst Prof Ahn Matae** matae.ahn@ntu.edu.sg https://dr.ntu.edu.sg/entities/person/Matae-Ahn
1.6	**Unravelling the brain-wide encoding of emotion states** How are emotions represented in the brain? The Nair lab at LKCMedicine investigates how neural circuits in the brain and AI models control and represent emotion states, including aggression and fear. This project will utilize new advances in high-density brain recordings in mice to understand the brain-wide encoding of complex emotion states. The student will work closely with AI experts in the group to model high-dimensional neural data as dynamical systems using interpretable	**Asst Prof Aditya Nair** aditya.nair@ntu.edu.sg https://www.nairlab.science

	AI techniques, building on prior work in the lab (Nair et al., Cell 2023, Vinograd*, Nair* et al., Nature 2024 and Nair et al., Science 2025). The ideal candidate will have a strong prior background in systems neuroscience techniques and experience in rodent neuroscience, including stereotaxic surgery.	
1.7	**Building a brain foundation model to predict and decode neural signals of emotion in mental health disorders** Can we predict a person's neural state from just their behavior? The Nair lab at LKCMedicine works at the intersection of neuroscience and AI and has been at the forefront of decoding neural signals of aggression and fear in the brain (see Nair et al., 2023 Cell and Nair et al., 2025 Science). In this project, the student will work with the lab to create a foundation model that is capable of predicting and decoding the neural signals underlying states of anger or fear from just behavioral measurements across species. This project has the potential to advance the development of "digital twins" of the brain, which could eventually enable personalized therapies based on individualized brain models capable of accurately predicting activity under disease and disorder states. The ideal candidate will possess a strong programming background and prior experience in handling neural datasets and deep learning frameworks such as PyTorch.	**Asst Prof Aditya Nair** aditya.nair@ntu.edu.sg https://www.nairlab.science
1.8	**Understanding the neural computation of emotion in foundation AI models and brain circuits** How are emotions represented in the brain and in deep neural networks? The Nair lab at LKCMedicine investigates how neural circuits in the brain and AI models control and represent emotion states, including aggression and fear. This project will utilize new advances in explainable and interpretable AI to reveal hidden neural computations in high-dimensional brain data and in foundation AI models including vision transformers Building on previous efforts from the lab (Nair et al., Cell 2023, Vinograd*, Nair* et al., Nature 2024 and Nair et al., Science 2025), the student will	**Asst Prof Aditya Nair** aditya.nair@ntu.edu.sg https://www.nairlab.science

	work at the intersection of neuroscience and machine learning to unravel the degree of similarity in how deep networks and brain circuits process emotion. The ideal candidate will possess a strong programming background and prior experience in handling neural datasets and deep learning frameworks such as PyTorch.	
1.9	**Building a deep learning system for high-throughput behavioral analysis of emotion states in models of neurodevelopmental disorders** How can we know if a person or animal is in a state of emotion? Building on recent advancements in computer vision from the Nair lab at LKCMedicine, this project will utilize new vision transformer models to predict behavioral states of emotion across species, from mice to humans. The student will work with the lab to train new multimodal large language models which can segment and create interpretable representations of diverse emotion states, including aggression. The student will also explore how behavioral representations of emotions are altered in animal models of neurodevelopmental disorders. This research has the potential to advance high throughput screening of drug targets and create a platform for behavioral phenotyping towards translational applications. The ideal candidate will possess a strong programming background and prior experience in handling neural datasets and deep learning frameworks such as PyTorch.	**Asst Prof Aditya Nair** aditya.nair@ntu.edu.sg https://www.nairlab.science
1.10	**Direct cell reprogramming for biomedical applications** ***Remarks: Project may be supported by scholarship funding*** The manufacture of advanced stem cell-based products and therapies through directed differentiation faces significant challenges in achieving efficient, reliable, and scalable production of specialized cell types especially in a cGMP setting. Cell differentiation approaches involve stepwise culture of (pluripotent) stem cells to direct their development into target cell	**Associate Prof Yen CHOO** yen.choo@ntu.edu.sg

	types. However, current manufacturing methods are generally not fit for purpose - being often hampered by complex, lengthy and costly protocols, low cell yield, purity and/or quality, and inconsistent outcomes - limiting industrial applications. Direct (or forward) cell programming offers a promising alternative by enabling the direct conversion of one cell type into another by activating gene regulatory networks that determine cell identity. This approach has the potential greatly to streamline the manufacturing process, reduce the time and resources required, and improve the consistency and functionality of cellular products. As the advanced therapy field develops, establishing robust, scalable manufacturing technology platforms (such as by direct cell programming) will become key to the success of the regenerative medicine and cell therapy industry. Programming of cells using lineage control networks has the potential to transform how we make cell therapies and immunotherapies, develop regenerative medicines, and create cellular models for research. However, identifying specific combinations of master regulatory genes known as transcription factors (TFs) that lead to highly efficient conversion of a scalable starting cell (e.g. iPSC, fibroblast) into desired cell types for biomedical applications (e.g. T cell, b cell) remains a significant challenge and a longstanding, critical bottleneck in the field. In this programme we will use an innovative combinatorial screening technology to rapidly assess the effectiveness of thousands of combinations of TFs in programming various human cell types into specific lineages that enable high value biomedical applications. Cell types we may derive in this project have diverse applications, including in: 1) developing advanced cellular/tissue models for biomedical R&D, 2) cGMP manufacturing of cell and gene therapies, including allogeneic immunotherapies, and 3) in vivo reprogramming for regenerative medicine and autologous immunotherapies.	
2. **Nutrition, Metabolism & Health**		

2.1	**Investigating the role of gut microbiome in cardiometabolic diseases** In recent years, it has become evident that the gut bacteria living in our intestine significantly impact health and disease. This influence extends beyond intestinal disorders like inflammatory bowel disease to encompass a wide range of conditions including obesity, diabetes, and neurodegenerative diseases. Our laboratory has previously reported that certain gut bacteria contributes to the progression of cardiovascular disease (PMID: 30397344, 37279756). This PhD project focuses on gut microbiota and lipid metabolism, employing state-of-the-art technologies such as anaerobic culture systems, mouse models, and next-generation sequencing to advance research in this field.	**Asst Prof Kazuyuki Kasahara** kazuyuki.kasahara@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp02039 https://kasaharalab.com
2.2	**Cardio-immunology: Elucidating the immune landscape of transplanted human cardiovascular progenitors in myocardial infarcted hearts** Ischemic heart failure is a non-communicable disease that affects a large number of individuals globally. A potential treatment that may enhance heart function and functionally replace injured cardiac muscles in cellular therapy. However, there is a gap in knowledge in understanding the immune rejection of xenograft after transplantation into myocardial infarcted hearts. Having this knowledge will be essential to devise strategies to target immune responses for a successful regenerative medicine therapy. This project aims to (1) transplant potentially hypo-immune human pluripotent stem cells (hPSCs) - derived cardiac progenitors into a MI mouse model and (2) map out the temporal immune landscape that led to graft rejection in a healthy and metabolic disease mouse model. The student will be working with cell and molecular techniques, differentiation and culture of hPSCs toward CVPs in preparation for transplanting into animals and downstream tissue processing. The	**Asst Prof Lynn Yap** lynn.yap@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp02163 https://www.linkedin.com/in/lynn-yap-39969879/

	study will focus on xenograft survival/rejection, immunology in healthy and metabolic MI animal models.	
2.3	**Unveiling the Hidden Impact of Microplastics on Metabolic Health: A Critical Research Frontier** Despite the alarming prevalence of microplastics, particularly in Southeast Asia which tops global intake, the short-term and long-term health impacts of these ubiquitous pollutants remain shrouded in mystery. This gap in knowledge is especially critical when considering the effects of microplastics on the development and progression of metabolic disorders—a vastly understudied area. With the world grappling with a metabolic syndrome pandemic and an urgent focus on metabolic health in the post-Covid era, unraveling how microplastics impact those with metabolic syndrome could be groundbreaking. The findings from such research promise to revolutionize our understanding and pave the way for transformative public health strategies. This work is highly interdisciplinary, integrating expertise from diverse fields to comprehensively understand the major types of microplastics present in dietary sources and everyday products. By employing human-relevant animal models of metabolic disorder and gut health, researchers can closely examine how these microplastics influence disease progression. This approach not only bridges gaps between environmental and material science, toxicology, and metabolic health but also promises to deliver insights that are directly applicable to human health, enhancing the relevance and impact of the findings. Candidate interested in this project should also apply for the Interdisciplinary Graduate Programme (IGP). Interdisciplinary Graduate Programme | Graduate College | NTU Singapore	**Assoc Prof Andrew Tan Nguan Soon** nstan@ntu.edu.sg **website** https://dr.ntu.edu.sg/cris/rp/rp00393 **Assoc Prof Dalton Tay Chor Yong (Co-sup)**

2.4	**Systematically Investigating Molecular Mechanisms Underlying Aging-Related Human Diseases through Multi-Omics Profiling** Aging is a complex biological process characterized by a gradual decline in physiological functions, which increases susceptibility to diseases and death. This process is influenced by a myriad of genetic, environmental, and lifestyle factors. To better understand aging and study the relationship between aging and aging-related diseases, our research group is focused on building predictive models using machine learning techniques. The model is to integrate multi-omics datasets, focusing specifically on gut microbiome and metabolomics data. The comprehensive analysis of these multi-omic datasets aims to unveil crucial molecular indicators, intricate biological pathways, and influential regulatory circuits that play a role in the aging process and the pathogenesis of age-associated disorders. Such an understanding is likely to be helpful in the development of innovative therapeutic interventions to promote healthy aging and to address the onset and progression of neurodegenerative conditions such as Alzheimer's and Parkinson's diseases.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
2.5	**Modulation of digestive enzyme activity as a safe approach to improve metabolism and health** This project aims to design new therapeutic targets, with structure-function lead optimisation of compounds that inhibit luminal carbohydrate enzymes. Guided by naturally occurring plant-based compounds, this project involves side-chain modifications to improve enzyme inhibition selectivity and specificity. From chemistry to biology, this project will continue with the characterization of luminal carbohydrate digestion modulation on the recipient host. Investigations will include an assessment of intestinal health, alterations in gut microbiome, impact on immunology and finally carbohydrate metabolism and homeostasis.	**Assoc Prof Yusuf Ali** Yusuf.ali@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp00609 **Assoc Prof Zaher Judeh** **(Co-sup)**

2.6	**Nutritional intervention and the impact on muscle health in elderly health** This project aims to molecularly dissect pathways that are altered under (i) intermittent fasting conditions and (ii) plant-based nutritional intake. These dietary interventions are increasingly being suggested as disease-modifiers, but the molecular mechanisms that support these claims are still not well-defined. With a focus on insulin sensitivity, immunology and metabolic organ homeostasis and health, the candidate will undertake a series of in vitro and in vivo experiments to understand the role of intracellular lipid regulation response to both dietary interventions. In collaboration with exercise physiologists from the National Institute of Education, candidate will also undertake a human study to validate translation and clinical relevance.	**Assoc Prof Yusuf Ali** Yusuf.ali@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp00609 **Assoc Prof Steven Burns** **(Co-sup)**
2.7	**In-vivo functional genetic screen to identify novel modulators of Non-Alcoholic Fatty Liver Disease (NAFLD)** The project focuses on employing in-vivo mouse models that resemble and recapitulate human disease to study NAFLD disease progression. Our preliminary results have identified several shRNAs that confer a negative or positive effect on the regenerative capacity of the hepatocytes. Further approach will be focused on validation of these shRNAs, such as their cell migration and cell proliferation characteristics using various in-vitro assays, followed by selection of the top performing shRNAs for in-vivo validation. In addition, combined transcriptomic and proteomic approaches will be undertaken to unravel new insights with the aim of identifying targets for therapeutic intervention and treatment of the disease.	**Assoc Prof Torsten Wuestefeld** Torsten.Wuestefeld@ntu.edu.sg
2.8	**Identification of novel senolytic targets for improving liver regeneration** The project focuses on conducting in vivo & in vitro functional genetic screens to identify targets to eliminate senescent cells. Senescent cells are known	**Assoc Prof Torsten Wuestefeld** Torsten.Wuestefeld@ntu.edu.sg

	to drive inflammaging attenuating the regenerative capacity of the liver. Through a negative selection screen in senescent cells we can identify vulnerabilities of these cells. The goal is to identify novel senolytic targets for therapeutic purposes.	
2.9	**Identifying novel biomarkers in liquid biopsy derived exosomes** The project focuses on identifying novel blood-based biomarkers for liver disease. Mouse models of chronic liver disease will be used, exosomes will be isolated from the blood and the content will be analyzed by transcriptomic and proteomic approaches. The same approach will be applied for liver patient derived blood samples. The goal is to identify novel conserved biomarkers for liver disease.	**Assoc Prof Torsten Wuestefeld** Torsten.Wuestefeld@ntu.edu.sg
2.10	**Ageing of bone microenvironments** Our skeletons play a crucial role in regulating key physiological processes, including mineral homeostasis, energy metabolism, and blood cell production. The presence of multiple blood vessel (BV) subtypes and the distinct microenvironments they support contribute to the skeleton's multifaceted functions. Vascular aging is a key factor in the age-related functional and physical changes observed in the skeleton. Understanding vascular niches and their age-related alterations could help target specific functional niches for managing age-related bone and blood diseases. In this study, we aim to identify and characterize bone vascular microenvironments and their functions. Leveraging cutting-edge techniques developed in our laboratory—including high-resolution 3D imaging, single-cell and spatial transcriptomics, metabolic analysis, and advanced mouse genetics—the candidate will have the opportunity to:	**Assoc Prof Saravana Kumar Ramasamy** saravana.kr@ntu.edu.sg

	• Characterize different types of microenvironments in bone. • Understand how blood vessels support these niches. • Identify strategies to replace or target aging blood vessel subtypes specifically.	
2.11	**Metabolic control of bone marrow microenvironments** The mammalian skeletal system undergoes continuous remodelling throughout life, intricately interacting with whole-body physiology. Metabolic changes significantly influence bone health by altering the cellular composition and functional dynamics of bone tissue. However, the cellular and molecular mechanisms underlying these dynamic changes remain poorly understood. In this study, we investigate the impact of metabolism on the mesenchymal composition of bone microenvironments. Specifically, the student will 1. Map and characterize the distribution patterns of mesenchymal cell subtypes in bone. 2. Explore how metabolic conditions such as diabetes, modulate mesenchymal cell composition 3. Identify metabolic targets to modulate mesenchymal cell differentiation and composition. The student will employ advanced techniques, including confocal and intravital imaging, single-cell and spatial transcriptomics, metabolic profiling, and state-of-the-art mouse transgenics. Overall, this study aims to uncover the mechanisms driving bone pathology in metabolic diseases like diabetes, providing a foundation for targeted therapeutic strategies.	**Assoc Prof Saravana Kumar Ramasamy** saravana.kr@ntu.edu.sg
2.12	**Deciphering the Role of Atypical LPS and MAMPs in Gut Barrier Dysfunction and MASLD** The gut barrier is a critical defense system, preventing harmful microbes and toxins from entering circulation	**Assoc Prof Andrew Tan Nguan Soon** nstan@ntu.edu.sg

	while supporting a balanced relationship with gut bacteria. When this barrier is compromised, it contributes to a cascade of chronic diseases. One of the most pressing concerns is Metabolic-Associated Steatotic Liver Disease (MASLD), a leading cause of chronic liver disease worldwide, which is increasingly linked to gut microbial imbalances. This PhD project will explore how microbe-associated molecular patterns (MAMPs), specifically classical and atypical lipopolysaccharides (LPS), influence gut barrier integrity via Angiopoietin-like protein 4 (Angptl4), a key regulator of lipid metabolism and inflammation. However, the precise molecular mechanisms by which these LPSs regulate Angptl4 remain unknown. Using cutting-edge microbiome analysis, biochemical characterization, and in vivo models, you will uncover how microbial signals shape gut-liver communication. The candidate will analyze bacterial LPS, assess receptor activation and gut permeability, and utilize germ-free mouse models. Why Join This Project? You'll gain expertise in host-microbe interactions, molecular biology, and immunology, with opportunities for clinical collaborations. Who Should Apply? We welcome applications from motivated candidates with a background in microbiology, molecular biology, immunology, bioinformatics, or a related field. A passion for host-microbe interactions and translational medicine is essential. Join us in uncovering how the gut microbiome influences metabolic disease and paving the way for microbiome-based therapeutics! References: Low, ZS, Chua, D., Cheng, H.S. et. al (2024). The LIDPAD Mouse Model Captures the Multisystem Interactions and Extrahepatic Complications in MASLD. Adv. Sci. 11(35): e2404326.	https://dr.ntu.edu.sg/cris/rp/rp00393
2.13	**Discovery of Gut Microbiome-Metabolized Bioactive Compounds from Traditional Chinese Medicine** We propose to culture human gut microbiomes with Traditional Chinese Medicine (TCM) extracts and apply a novel computational algorithm to identify new	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg

	bioactive compounds metabolized by the microbiota. This integrative platform enables systematic discovery of microbiome-derived metabolites from natural products, uncovering mechanisms underlying TCM efficacy and revealing potential therapeutic agents. Beyond discovery, we aim to construct a comprehensive atlas of gut microbiome-metabolized TCM and natural products. This resource will serve as a foundation for drug development and precision therapeutics based on host–microbe–metabolite interactions.	**Website** Shen Lab (shen-lab.org)
2.14	**Metabolic feature-based functional module analysis based on the large language model** We propose to develop featureFMA, a novel large language model (LLM)-guided computational framework for metabolic feature-based functional module analysis in LC-MS untargeted metabolomics. Traditional pathway analysis lacks specificity and coverage for metabolomics data. featureFMA will integrate metabolite annotation, metabolic network modeling, and LLM-based functional interpretation to identify dysregulated modules linked to biological functions and diseases. This project includes software development (R package, Shiny app, and cloud platform), multi-species validation, and diverse case studies (e.g., enzyme mutation and gut microbiome). featureFMA will provide a scalable, intelligent solution for interpreting complex metabolomics data and accelerating functional discovery in systems biology.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
2.15	**Bat-inspired targets to fight human diseases and aging** The objective is to learn from bats with exceptional disease resistance and healthy longevity, aiming to translate these lessons into new targets to fight human diseases and extend healthspan. The pioneering work in bat inflammation (*Nat Micro* 2019, *PNAS* 2020, *Nature* 2021, *Cell* 2023 and ongoing development of a new class of anti-inflammatory drugs) has helped establish bats as a great model to uncover new strategies to fight human diseases and has just scratched the surface of what we can learn from bats to benefit humans. The three different and synergistic approaches include 1) 'unbiased' multi-omics aging atlas of bats 2) 'disease centric' disease-free bat models including metabolic and neurological diseases	**Asst Prof Ahn Matae** matae.ahn@ntu.edu.sg https://dr.ntu.edu.sg/entities/person/Matae-Ahn

	and 3) 'more targeted' study of enhanced proliferation/regeneration and increased apoptosis as potential anti-aging/cancer mechanisms.	
2.16	**The contribution of genetics to dietary habit and its relation to adiposity and cardiometabolic diseases in multiethnic Asian population** Excess visceral adiposity promotes adverse cardiometabolic outcomes1, is elevated in people of Asian ancestries, and is likely to be largely influenced by non-genetic, including dietary habit. Large-scale Genome-Wide Association Studies (GWAS) has demonstrated the genetic contribution towards dietary habit2. We want to: 1) understand how the genetic variation is associated with dietary habit, particularly macronutrient intake, in the multi-ethnic Asian population and 2) to determine the causal evidence linking genetic predisposition for macronutrient intake **Reference:** 1. Mina, et al. Adiposity and metabolic health in Asian populations: an epidemiological study using dual-energy x-ray absorptiometry in Singapore. The Lancet Diabetes & Endocrinology, Volume 12, Issue 10, 704 – 715. http://doi.org/10.1016/S2213-8587(24)00195-5. 2. Meddens, et al. Genomic analysis of diet composition finds novel loci and associations with health and lifestyle. Mol Psychiatry (2020). https://doi.org/10.1038/s41380-020-0697-5. 3.https://www.npm.sg/files/PRECISE_SG100K_Flagship_and_Driver_Projects_revised.pdf and visceral adiposity, independent of linked cardiometabolic traits. We will leverage on the approved driver project of the PRECISE-SG100K Study3, as well as other publicly available GWAS data. Experience in GWAS, use of CLI or Cloud systems will be advantageous.	**Asst Prof Theresia Mina** Theresia.hm@ntu.edu.sg https://www.researchgate.net/profile/Theresia-Mina
2.17	**The role of eating behaviour in cardiometabolic health in Asian Population** Suboptimal dietary habit and underlying eating behaviour are risk factors for excess adiposity. We hypothesise that adverse eating behaviour and dietary	**Asst Prof Theresia Mina** Theresia.hm@ntu.edu.sg

	habit contribute to excess visceral adiposity and cardiometabolic disease burden in the Asian population. In this project, we aim to i) comprehensively quantify eating behaviour using validated questionnaires in 900 multi-ethnic Asians using Theoretical Domain Framework[1] and ii) identify eating behavioural risk factors that promote excess adiposity in the multiethnic Asian population through epidemiological investigations using high-throughput approach such as Phenome-wide Association Studies (PheWAS)[2]. We will leverage on the ongoing AETSCAPE Study that has collected >500 eating behavioural dataset from the SG100K-HELIOS Study participants and the approved data linkage with the comprehensive HELIOS Study lifestyle and health data. Experience in statistical programming will be advantageous. **Reference:** 1. Atkins L, et al. Implementation Science 2017; 12. DOI:10.1186/s13012-017-0605-9. 2. Mina, et al. Brief Communications: Phenome-wide Association Study of Cognitive Function in Multiethnic Asian population. MedRxiV https://doi.org/10.1101/2025.06.18.25329738	https://www.researchgate.net/profile/Theresia-Mina
2.18	**Direct cell reprogramming for biomedical applications** ***Remarks: Project may be supported by scholarship funding*** The manufacture of advanced stem cell-based products and therapies through directed differentiation faces significant challenges in achieving efficient, reliable, and scalable production of specialized cell types especially in a cGMP setting. Cell differentiation approaches involve stepwise culture of (pluripotent) stem cells to direct their development into target cell types. However, current manufacturing methods are generally not fit for purpose - being often hampered by complex, lengthy and costly protocols, low cell yield, purity and/or quality, and inconsistent outcomes - limiting industrial applications. Direct (or forward) cell programming offers a promising alternative by enabling the direct conversion	**Associate Prof Yen CHOO** yen.choo@ntu.edu.sg

	of one cell type into another by activating gene regulatory networks that determine cell identity. This approach has the potential greatly to streamline the manufacturing process, reduce the time and resources required, and improve the consistency and functionality of cellular products. As the advanced therapy field develops, establishing robust, scalable manufacturing technology platforms (such as by direct cell programming) will become key to the success of the regenerative medicine and cell therapy industry. Programming of cells using lineage control networks has the potential to transform how we make cell therapies and immunotherapies, develop regenerative medicines, and create cellular models for research. However, identifying specific combinations of master regulatory genes known as transcription factors (TFs) that lead to highly efficient conversion of a scalable starting cell (e.g. iPSC, fibroblast) into desired cell types for biomedical applications (e.g. T cell, b cell) remains a significant challenge and a longstanding, critical bottleneck in the field. In this programme we will use an innovative combinatorial screening technology to rapidly assess the effectiveness of thousands of combinations of TFs in programming various human cell types into specific lineages that enable high value biomedical applications. Cell types we may derive in this project have diverse applications, including in: 1) developing advanced cellular/tissue models for biomedical R&D, 2) cGMP manufacturing of cell and gene therapies, including allogeneic immunotherapies, and 3) in vivo reprogramming for regenerative medicine and autologous immunotherapies.	
	3. **Population & Global Health**	
3.1	**Comprehensive Multi-omics Analysis of Human Aging Using the Large Language Module based Functional Module Annotation** Multi-omic methods provide great opportunities to systematically reveal the critical molecular alterations of aging from a multidimensional perspective, while matching and investigating the biological information	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website**

	and functions from multi could be a heavy subjective work. Large Language Models (LLMs) has shown high efficiency and accuracy in repetitive search and collection work, which will help us to extensively and quickly investigate potential research objects and validate them with published works to prove their roles and molecular mechanism. So in this project, we aim to build up a tool utilizing LLM, such as GPT4, to accelerate and improve the biological investigation in multi-omics data for aging research.	Shen Lab (shen-lab.org)
3.2	**Climate and health – mapping the impacts towards positive action** This PhD is located within a wider multidisciplinary project NTU "Climate Transformation Program" that seeks to map and model impacts of climate change. World Health Organization (WHO) emphatically noted that the risks of the climate crisis to human health extend way beyond physical impact(s) to mental health and called for intervention(s), mitigation and adaptation. The evidence however on mental health impacts in Singapore and Southeast Asia is limited. The PHD project will integrate evidence synthesis and observational mixed methods approached to identify mental health risks and at risk populations.	**Assoc Prof Konstadina Griva** Konstadina.griva@ntu.edu.sg https://earthobservatory.sg/research/climate climate-transformation-programme **Co-supervisor:** **Assoc Prof Steve Yim**
3.3	**Mapping and Optimising Public involvement in Biobanks** Biobanks play an important and emerging role in supporting basic and translational research. The PHD project will be nested in a population cohort study (HELIOS; https://www.healthforlife.sg), established and led by Lee Kong Chian School of Medicine that aims to identify environmental, lifestyle and genetic factors that cause heart disease, diabetes, cancer and other chronic diseases in Singapore. The work will seek (a) to sunthesise evidence on Patient Public Involvement in context of biobanks; (b) to develop implement and evaluate Patient Public Involvement initiatives and (c) to conduct mixed methods study related to return of results procedures. The work will involve scoping literature reviews, preparatory work for evaluation studies including public and community	**Assoc Prof Konstadina Griva** Konstadina.griva@ntu.edu.sg **Co-supervisor:** **Prof John Chambers**

	involvement and engagement activities, collection analysing qualitative and quantitative data, building relationships with relevant stakeholders.	
3.4	**Ageing of bone microenvironments** Our skeletons play a crucial role in regulating key physiological processes, including mineral homeostasis, energy metabolism, and blood cell production. The presence of multiple blood vessel (BV) subtypes and the distinct microenvironments they support contribute to the skeleton's multifaceted functions. Vascular aging is a key factor in the age-related functional and physical changes observed in the skeleton. Understanding vascular niches and their age-related alterations could help target specific functional niches for managing age-related bone and blood diseases. In this study, we aim to identify and characterize bone vascular microenvironments and their functions. Leveraging cutting-edge techniques developed in our laboratory—including high-resolution 3D imaging, single-cell and spatial transcriptomics, metabolic analysis, and advanced mouse genetics—the candidate will have the opportunity to: • Characterize different types of microenvironments in bone. • Understand how blood vessels support these niches. • Identify strategies to replace or target aging blood vessel subtypes specifically.	**Assoc Prof Saravana Kumar Ramasamy** saravana.kr@ntu.edu.sg
3.5	**Metabolic control of bone marrow microenvironments** The mammalian skeletal system undergoes continuous remodelling throughout life, intricately interacting with whole-body physiology. Metabolic changes significantly influence bone health by altering the cellular composition and functional dynamics of bone tissue. However, the cellular and molecular	**Assoc Prof Saravana Kumar Ramasamy** saravana.kr@ntu.edu.sg

	mechanisms underlying these dynamic changes remain poorly understood. In this study, we investigate the impact of metabolism on the mesenchymal composition of bone microenvironments. Specifically, the student will 1. Map and characterize the distribution patterns of mesenchymal cell subtypes in bone. 2. Explore how metabolic conditions such as diabetes, modulate mesenchymal cell composition 3. Identify metabolic targets to modulate mesenchymal cell differentiation and composition. The student will employ advanced techniques, including confocal and intravital imaging, single-cell and spatial transcriptomics, metabolic profiling, and state-of-the-art mouse transgenics. Overall, this study aims to uncover the mechanisms driving bone pathology in metabolic diseases like diabetes, providing a foundation for targeted therapeutic strategies.	
3.6	**Understanding the tumor microenvironment: High-resolution 3D and multiplex imaging approach for deciphering cancer progression** Endothelial cells are pivotal architects of blood and lymphatic vessel integrity, forming the inner lining that regulates inflammation, immune cell trafficking, and organ-specific vascular functions. Perivascular and mesenchymal stromal cells dynamically shape vascular microenvironments, playing essential roles in tissue homeostasis and disease. In cancer, the tumor microenvironment (TME) drives disease progression by orchestrating a complex interplay among cancer cells, vascular networks, and stromal components. This dynamic milieu enhances metastatic potential and contributes to therapeutic resistance. Central to this process is epithelial-mesenchymal transition (EMT), which equips cancer cells with invasive properties. Critically, stromal and vascular cells are key enablers of EMT and therapy resistance, making them highly attractive targets for innovative therapeutic strategies.	**Assoc Prof Anjali Parmanand Kusumbe** anjali.pkusumbe@ntu.edu.sg https://dr.ntu.edu.sg/cris/rp/rp02539

	Despite their significance, the complexity, heterogeneity, and spatial interactions of tumor stroma and vasculature remain poorly understood across different stages of cancer progression. This knowledge gap limits the development of precision therapies. To address this challenge, we propose leveraging cutting-edge high-resolution light-sheet microscopy and multiplex imaging to define, at an unprecedented level, the spatial interactions between vascular, stromal, and cancer cells throughout disease progression. Our approach focuses on three malignancies with distinct clinical and biological challenges: head and neck cancers, glioblastoma, and breast tumors. This study aims to illuminate the spatial interactions within the TME, providing a foundation not only for the development of targeted interventions to disrupt the stromal-vascular axis in cancer progression but also for precise diagnostic and prognostic strategies throughout the course of the disease.	
3.7	**Discovery of Gut Microbiome-Metabolized Bioactive Compounds from Traditional Chinese Medicine** We propose to culture human gut microbiomes with Traditional Chinese Medicine (TCM) extracts and apply a novel computational algorithm to identify new bioactive compounds metabolized by the microbiota. This integrative platform enables systematic discovery of microbiome-derived metabolites from natural products, uncovering mechanisms underlying TCM efficacy and revealing potential therapeutic agents. Beyond discovery, we aim to construct a comprehensive atlas of gut microbiome-metabolized TCM and natural products. This resource will serve as a foundation for drug development and precision therapeutics based on host–microbe–metabolite interactions.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
3.8	**Optimising cancer screening in primary care** Cancer is the leading cause of death in Singapore, with three in 10 people expected to die of the condition. When cancer is diagnosed earlier, treatment is more effective and costs less, while survival rates increase and carer quality of life is improved. Cancer screening aims to detect early stage cancer to realise these benefits, however screening uptake is currently suboptimal in Singapore. This PhD will explore	**Assoc Prof Jo-Anne Elizabeth Manski-Nankervis** joanne.mn@ntu.edu.sg **Website** https://www.ntu.edu.sg/pcfm

	development and implementation of a multicancer risk tool to communicate risk of cancer and facilitate appropriate screening.	
3.9	**Can polygenic risk scores be used to facilitate cancer screening in primary care?** Polygenic risk scores have been proposed as a solution to stratify cancer risk, resulting in tailoring of screening recommendations in order to increase the detection of cancers in those at younger age, reduce risks associated with false positives and reduce harms associated with unnecessary biopsies and invasive treatments. This PhD will explore acceptability and feasibility of polygenic risk scores for risk stratification of cancer screening in primary care. This will inform future implementation with the aim of combining the reach of primary health care with Singapore's goal of achieving precision medicine to overcome the challenge of late cancer diagnosis related to suboptimal breast cancer and colorectal cancer screening.	**Assoc Prof Jo-Anne Elizabeth Manski-Nankervis** joanne.mn@ntu.edu.sg **Website** https://www.ntu.edu.sg/pcfm
3.10	**Implementation of a family history tool in primary care to identify people that may benefit from predictive genetic testing in primary care** Primary care roles in health assessment, screening, early detection and prevention have been strengthened by HealthierSG strategy. With genetic testing expected to transform the practice of medicine in the next 10 years, there is a need to explore effective implementation of clinical workflows in primary care. The estimated prevalence of familial hypercholesterolaemia (FH) in Singapore is 1 in 140 people; Approximately 1 in 150 Singaporeans carry a pathogenic variant of hereditary breast and ovarian cancer syndrome (HBOC), and 1 in 530 have a pathogenic variant of Lynch syndrome. However, the majority of carriers in the population are not identified until they actually develop one of the conditions associated with the genetic variant. Recording of family history is primary care needs to be optimised to identify people that may benefit from predictive genetic testing.	**Assoc Prof Jo-Anne Elizabeth Manski-Nankervis** joanne.mn@ntu.edu.sg **Website** https://www.ntu.edu.sg/pcfm

	This PhD will involve the development of clinical workflows, incorporating a digital family history self-completion tool for patients, exploring key determinants of behavioural intention towards genetic testing through a survey; and development and evaluation of customized genetic risk communication strategies in shaping outcomes in primary care settings.	
3.11	**HealthierSG in private general practice: opportunities and challenges** HealthierSG aims to encourage and facilitate healthier living amongst Singaporeans. This includes promoting regular exercise, a balanced diet, mental well-being, and regular health screenings. Private general practices, where 80% of family doctors work, will play a key role in ensuring the success of HealthierSG. This PhD will explore the experiences of GPs and patients attending private general practice in relation to HealthierSG and explore models of care that facilitate chronic disease and preventive health outcomes.	**Assoc Prof Jo-Anne Elizabeth Manski-Nankervis** joanne.mn@ntu.edu.sg **Website** https://www.ntu.edu.sg/pcfm
3.12	**Metabolic feature-based functional module analysis based on the large language model** We propose to develop featureFMA, a novel large language model (LLM)-guided computational framework for metabolic feature-based functional module analysis in LC-MS untargeted metabolomics. Traditional pathway analysis lacks specificity and coverage for metabolomics data. featureFMA will integrate metabolite annotation, metabolic network modeling, and LLM-based functional interpretation to identify dysregulated modules linked to biological functions and diseases. This project includes software development (R package, Shiny app, and cloud platform), multi-species validation, and diverse case studies (e.g., enzyme mutation and gut microbiome). featureFMA will provide a scalable, intelligent solution for interpreting complex metabolomics data and accelerating functional discovery in systems biology.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)

3.13	**Sustainable Precision Healthcare: Predictive Modelling and Global Strategies for Environmentally Linked Diseases** ***Remarks: Project may be supported by scholarship funding*** Precision healthcare promises to transform disease prevention, diagnosis, treatment and prognosis by tailoring interventions to individual risk profiles. However, its adoption faces challenges of cost, feasibility, and contextual relevance. This research addresses these gaps by: (1) developing and evaluating predictive modelling frameworks for environmentally dependent diseases including respiratory illnesses; (2) quantifying the incremental predictive and clinical value of biomarkers, molecular signatures, phenotypes, endotypes, and external determinants including environmental exposures and socio-economic risks; and (3) assessing implementation feasibility and implications across high-income and low- and middle-income countries. The findings will provide evidence to guide equitable and sustainable precision healthcare strategies globally.	**Dr Michele Nguyen** michele.nguyen@ntu.edu.sg **Website** www.drmichelenguyen.com **Co-Supervisor:** Assoc Prof Sanjay Chotirmall Asst Prof Liang Yao
3.14	**The "Burden of Evidence" in Respiratory and Infectious Medicine: Quantifying the Impact of Low-Quality Research on Health Equity and AI Integrity** ***Remarks: Project may be supported by scholarship funding*** The annual output of MEDLINE-indexed articles now exceeds one million, creating a paradox where more information often leads to less clarity. Medical knowledge increasingly reaches clinicians through fragmented feeds designed for engagement rather than accuracy. This phenomenon has created a "burden of evidence." Analogous to the "burden of disease," this concept measures the systemic prevalence of low-quality, biased, and redundant research. This burden is not merely a waste of resources; it is an active pollutant in the healthcare ecosystem that distorts clinical guidelines, threatens health equity, and poisons the datasets used to train the next generation of medical Artificial Intelligence (AI).	**Dr Liang Yao** Liang.yao@ntu.edu.sg **Website** https://www.liamyao.com/ **Co-Supervisor:** Asst Prof Michele Nguyen Assoc Prof Sanjay Chotirmall

	To address this, we must shift from celebrating research volume to interrogating its integrity. This PhD project aims to quantify and characterize the burden of evidence specifically within Respiratory and Infectious Diseases—a field critically impacted by rapid, high-volume publication cycles. The research will proceed in two objectives: (1) Primary Research Assessment: Systematically evaluate the prevalence of "high risk of bias" in pivotal randomized controlled trials and observational studies within the field. (2) Synthesis quality qssessment: Determine the proportion of evidence summaries (systematic reviews and meta-analyses) that are proved as low-certainty evidence to form conclusions. (3) Impact and uptake analysis: Trace the downstream penetration of this low-quality evidence by quantifying how frequently these flawed studies are cited in major clinical guidelines and policy documents. By mapping the extent of this "evidence burden" this project will provide a framework to decontaminate clinical decision-making and ensure that future health policies and AI tools are built upon a foundation of trustworthy data.	
	4. Respiratory & Infectious Diseases	
4.1	**Exploring RNA Viral Vectors for mRNA Therapy Applications** This project aims to investigate the molecular mechanisms of RNA viral vectors and their implications in developing next-generation mRNA therapies for infectious diseases, cancer, and other chronic conditions. Leveraging the unique properties of RNA viral vectors, such as high transfection efficiency and low immunogenicity, we propose to systematically characterize the vector-host interactions at the molecular level. This will involve the use of cutting-edge biotechnological tools, including CRISPR-Cas9 genome editing and next-generation sequencing, to optimize vector design and functionality. By elucidating the molecular basis of RNA viral vector-mediated mRNA delivery, this research intends to pave the way for highly effective and targeted therapies. The outcomes are expected to have profound impacts on	**Assoc Prof Luo Dahai** **luodahai@ntu.edu.sg** **Website** https://www.ntu.edu.sg/research/faculty-directory/detail/rp00464

	the treatment strategies for a wide range of diseases, enhancing the therapeutic efficacy while minimizing adverse effects.	
4.2	**Molecular Basis of the Flavivirus Replication Process** Dengue is a critical public health issue with severe forms affecting hundreds of thousands annually. Without a vaccine offering lasting protection against all DENV serotypes, treatment relies on symptomatic care and antivirals. The replication of the virus involves a complex known as the replication complex (RC), which is central to viral replication and a prime target for drug development. Despite advances in understanding individual components of the RC, its full architecture and interactions remain elusive. his project aims to uncover key protein-protein and protein-RNA interactions within the DENV RC using methods from biochemistry, biophysics, structural biology, cell biology, and virology. Approaches include reconstituting the RC with selected proteins and isolating it from infected cells to study its composition and functionality.	**Assoc Prof Luo Dahai** luodahai@ntu.edu.sg **Website** https://www.ntu.edu.sg/research/faculty-directory/detail/rp00464
4.3	**Effects of host and environment in shaping the lipid coat of Gram negative bacterium** Gram negative bacterium (GNB) is well protected from its environment by its dual membrane. This barrier is one of the key factors for bacterial resistance to the actions of antimicrobials. In this study, we seek to understand how the environment and the host shapes the lipids of GNB, and the phenotypic effects, including virulence and antimicrobial resistance. The works will facilitate discovery of therapeutic strategies for fighting infections.	**Asst Prof Guan Xueli** xueli.guan@ntu.edu.sg
4.4	**Understanding lipid variations in carbapenem-resistant *Klebsiella pneumoniae*** Carbapenem-resistant *K. pneumoniae* (CRKP) is a global and local health threat. Whole genome sequencing of clinical isolates have greatly facilitated	**Asst Prof Guan Xueli** xueli.guan@ntu.edu.sg

	the discovery of antimicrobial resistance mechanisms, and transmission. However, there remained a discordance between the genetics of the bacterium and its phenotypes. This project will explore the underlying basis of lipid variations clinical CRKP, and the impact on antimicrobial resistance in *K. pneumoniae.*	
4.5	***Protein Lipidation (S-acylation) in Membrane Damage during Infection and Immunity*** Cell membranes are highly vulnerable to oxidative stress that damages organelles and threatens cell viability. Such membrane damage is a hallmark of infection, neurodegeneration, and inflammatory disease. We discovered that cells counteract lipid damage through a transcriptional and epigenetic program that promotes detoxification and innate immunity (accepted Nat. Commun. 2025). A key component of this response is the reversible switch of protein fatty acid acylation, which regulates central aspects of cell biology, contributes to innate immune defense, and directly influences SARS-CoV-2 infection. This project will investigate the links between membrane lipid damage, protein lipidation, and innate immunity. Using genetic screens, transcriptomics, molecular and chemical biology, and advanced imaging, we will identify cellular sensors of lipid damage, define their protective roles in infection, and evaluate protein lipidation as a host-directed therapeutic target. *Relevant Publications (Mesquita et al):* *https://www.biorxiv.org/content/10.1101/2025.02.25.640160v2* *https://www.nature.com/articles/s41467-023-43027-2* *https://infoscience.epfl.ch/entities/patent/de39ac78-a6d5-418d-a6fa-5bdb09775e5a*	**Asst Prof Francisco Sarmento Mesquita** **https://www.mesquitalab.com**
4.6	***How Viruses Remodel Host Membranes*** Enveloped RNA viruses such as SARS-CoV-2 remodel host membranes to assemble infectious virions and to build replication organelles. Viral structural proteins	**Asst Prof Francisco Sarmento Mesquita** **https://www.mesquitalab.com**

	undergo extensive S-acylation, a lipid modification that we showed is critical for SARS-CoV-2, as it regulates Spike protein function, virion lipid composition, and infectivity. These findings raise fundamental questions about how protein lipidation and membrane remodeling shape host–virus interactions. This project will investigate how viruses select and reorganize host lipids to support envelope biogenesis and replication. We will combine mutagenesis of viral proteins, viral expression systems, lipidomics and proteomics, structural studies, and high-resolution imaging of infection to uncover conserved principles of viral membrane remodeling and identify host factors that may be targeted for antiviral intervention. *Relevant Publications (Mesquita et al):* *DOI: 10.1016/j.devcel.2021.09.016* *https://www.nature.com/articles/s41467-023-35921-6*	
4.7	**Sustainable Precision Healthcare: Predictive Modelling and Global Strategies for Environmentally Linked Diseases** ***Remarks: Project may be supported by scholarship funding*** Precision healthcare promises to transform disease prevention, diagnosis, treatment and prognosis by tailoring interventions to individual risk profiles. However, its adoption faces challenges of cost, feasibility, and contextual relevance. This research addresses these gaps by: (1) developing and evaluating predictive modelling frameworks for environmentally dependent diseases including respiratory illnesses; (2) quantifying the incremental predictive and clinical value of biomarkers, molecular signatures, phenotypes, endotypes, and external determinants including environmental exposures and socio-economic risks; and (3) assessing implementation feasibility and implications across high-income and low- and middle-income countries. The findings will provide evidence to guide equitable and sustainable precision healthcare strategies globally.	**Dr Michele Nguyen** michele.nguyen@ntu.edu.sg **Website** www.drmichelenguyen.com **Co-Supervisor:** Assoc Prof Sanjay Chotirmall Asst Prof Liang Yao

4.8	**The "Burden of Evidence" in Respiratory and Infectious Medicine: Quantifying the Impact of Low-Quality Research on Health Equity and AI Integrity** ***Remarks: Project may be supported by scholarship funding*** The annual output of MEDLINE-indexed articles now exceeds one million, creating a paradox where more information often leads to less clarity. Medical knowledge increasingly reaches clinicians through fragmented feeds designed for engagement rather than accuracy. This phenomenon has created a "burden of evidence." Analogous to the "burden of disease," this concept measures the systemic prevalence of low-quality, biased, and redundant research. This burden is not merely a waste of resources; it is an active pollutant in the healthcare ecosystem that distorts clinical guidelines, threatens health equity, and poisons the datasets used to train the next generation of medical Artificial Intelligence (AI). To address this, we must shift from celebrating research volume to interrogating its integrity. This PhD project aims to quantify and characterize the burden of evidence specifically within Respiratory and Infectious Diseases—a field critically impacted by rapid, high-volume publication cycles. The research will proceed in two objectives: (1) Primary Research Assessment: Systematically evaluate the prevalence of "high risk of bias" in pivotal randomized controlled trials and observational studies within the field. (2) Synthesis quality assessment: Determine the proportion of evidence summaries (systematic reviews and meta-analyses) that are proved as low-certainty evidence to form conclusions. (3) Impact and uptake analysis: Trace the downstream penetration of this low-quality evidence by quantifying how frequently these flawed studies are cited in major clinical guidelines and policy documents. By mapping the extent of this "evidence burden" this project will provide a framework to decontaminate clinical decision-making and ensure that future health policies and AI tools are built upon a foundation of trustworthy data.	**Dr Liang Yao** Liang.yao@ntu.edu.sg **Website** https://www.liamyao.com/ **Co-Supervisor:** Asst Prof Michele Nguyen Assoc Prof Sanjay Chotirmall
4.9	**Direct cell reprogramming for biomedical applications** ***Remarks: Project may be supported by scholarship funding***	**Associate Prof Yen CHOO** yen.choo@ntu.edu.sg

	The manufacture of advanced stem cell-based products and therapies through directed differentiation faces significant challenges in achieving efficient, reliable, and scalable production of specialized cell types especially in a cGMP setting. Cell differentiation approaches involve stepwise culture of (pluripotent) stem cells to direct their development into target cell types. However, current manufacturing methods are generally not fit for purpose - being often hampered by complex, lengthy and costly protocols, low cell yield, purity and/or quality, and inconsistent outcomes - limiting industrial applications. Direct (or forward) cell programming offers a promising alternative by enabling the direct conversion of one cell type into another by activating gene regulatory networks that determine cell identity. This approach has the potential greatly to streamline the manufacturing process, reduce the time and resources required, and improve the consistency and functionality of cellular products. As the advanced therapy field develops, establishing robust, scalable manufacturing technology platforms (such as by direct cell programming) will become key to the success of the regenerative medicine and cell therapy industry. Programming of cells using lineage control networks has the potential to transform how we make cell therapies and immunotherapies, develop regenerative medicines, and create cellular models for research. However, identifying specific combinations of master regulatory genes known as transcription factors (TFs) that lead to highly efficient conversion of a scalable starting cell (e.g. iPSC, fibroblast) into desired cell types for biomedical applications (e.g. T cell, b cell) remains a significant challenge and a longstanding, critical bottleneck in the field. In this programme we will use an innovative combinatorial screening technology to rapidly assess the effectiveness of thousands of combinations of TFs in programming various human cell types into specific lineages that enable high value biomedical applications. Cell types we may derive in this project have diverse applications, including in: 1) developing advanced cellular/tissue models for biomedical R&D, 2) cGMP manufacturing of cell and gene therapies,	

	including allogeneic immunotherapies, and 3) in vivo reprogramming for regenerative medicine and autologous immunotherapies.	
	5. Skin Disease & Wound Repair	
5.1	**The role of microtrauma in human hair regrowth and regeneration** Androgenetic alopecia (or male pattern baldness) affects more than half of men by the time they reach middle age, whereby hair follicles miniaturise over time. We currently do not understand the mechanism of the human hair cycle, or how to reverse miniaturization. The popularity of treatments like microneedling suggest that subclinical wounding (ie. Microtrauma) has a role in allowing hair follicle stem cells and their microenvironment to regenerate. Our team is focused on understanding the basic mechanisms of microtrauma on human skin and hair follicles, and translating these findings into exciting new treatments for hair loss.	**Co-Supervisor:** **Asst Prof Etienne Wang** etienne@nsc.com.sg
5.2	**Post-Translational Modifications of the Integrin LFA-1 in the Regulation of T-Cell Motility** Leukocyte function-associated antigen-1 (LFA-1) is an integrin expressed on T-cells and plays a crucial role in T-cell signaling, adhesion, and motility. Protein post-translational modifications are known to influence integrin functions. However, LFA-1 post-translational modifications and their functional roles are not clearly understood. This project aims to determine the impact of glycosylation and sulfation on LFA-1 activation, clustering, and signaling, investigate how these post-translation modifications affect T-cell motility. The outcomes of this research will provide deep insights into the molecular mechanisms that underpin T-cell immunology, which could lead to developing novel and safe strategies to fine tune T-cell function.	**Assoc Prof Navin Kumar Verma** nkverma@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp00490
5.3	**Understanding the Role of DDX3 in Lymphoma Drug Resistance**	**Assoc Prof Navin Kumar Verma**

	Despite the use of multi-agent chemotherapy for non-Hodgkin lymphoma, treatment outcomes remain poor due to the development of chemoresistance and high relapse rates. We have recently reported that loss-of-function mutations in the X-linked RNA helicase DDX3X are associated with chemoresistance and poor prognosis in non-Hodgkin lymphoma subtypes. This project aims to further investigate DDX3X involvement in Epstein-Barr virus (EBV)-associated Natural killer/T-cell lymphoma (NKTCL), which is an Asian-prevalent aggressive subtype. The outcomes will advance our understanding of non-Hodgkin lymphoma disease mechanism and drug resistance that would have profound impact on treatment strategies.	nkverma@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp00490
5.4	**Design of microneedle for skin tissue health and disease profiling** The skin, being the largest organ of the body that interfaces with the external environment, offers an excellent site for drug administration (injection) and retrieval of human biological materials (blood draw). Microneedles are medical devices that comprises of an array of micron-sized needles, designed to overcome the physical barrier imposed by the outer most layer of skin (stratum corneum). Owing to their minimally-invasiveness, relatively pain-free application and ease of use, they have emerged as attractive options for both cutaneous delivery and the collection of biological samples for health monitoring. Herein, we aim to leverage on the speed and versatility of additive manufacturing to fabricate microneedles with features that are tailored for the extraction of biospecimens, such as microbiome, interstitial fluid and nucleic acids from the host human skin tissue, which will offer a simple and patient-friendly method for the prediction and diagnosis of skin health and disease.	**Asst Prof Liang Kun** kun.liang@ntu.edu.sg **Website** www.klianglab.com
5.5	**Therapeutic marine collagen hydrogels for skin repair and rejuvenation** The skin, being the tissue that forms the main interface with the external environment, is prone to various insults and injuries including wounds, natural aging, and ultraviolet-induced damage. Hence there is increasing interest in developing strategies for skin	**Asst Prof Liang Kun** kun.liang@ntu.edu.sg **Website**

	repair and rejuvenation. Collagen, which is the main component of our dermal extracellular matrix, has been traditionally used for such purposes. Nevertheless, commercially available mammalian collagen has limitations such as zoonotic disease transmission and religious restrictions. To address these challenges, we have developed a scalable process to extract purified collagen from fish skin and demonstrated the ability to support skin regeneration *in vitro*. Herein we aim to investigate the supplementation of the collagen hydrogels with therapeutic moieties that deliver photo and/or electrical stimulation to enhance skin repair *in vivo.* We hypothesize that the anti-inflammatory and antioxidative properties conferred by these hydrogels can decrease proinflammatory cytokines and reduce oxidative damage, leading to accelerated skin repair and rejuvenation of ageing skin.	www.klianglab.com
5.6	**Direct cell reprogramming for biomedical applications** ***Remarks: Project may be supported by scholarship funding*** The manufacture of advanced stem cell-based products and therapies through directed differentiation faces significant challenges in achieving efficient, reliable, and scalable production of specialized cell types especially in a cGMP setting. Cell differentiation approaches involve stepwise culture of (pluripotent) stem cells to direct their development into target cell types. However, current manufacturing methods are generally not fit for purpose - being often hampered by complex, lengthy and costly protocols, low cell yield, purity and/or quality, and inconsistent outcomes - limiting industrial applications. Direct (or forward) cell programming offers a promising alternative by enabling the direct conversion of one cell type into another by activating gene regulatory networks that determine cell identity. This approach has the potential greatly to streamline the manufacturing process, reduce the time and resources required, and improve the consistency and functionality of cellular products. As the advanced therapy field develops, establishing robust, scalable manufacturing technology platforms (such as by direct	**Associate Prof Yen CHOO** yen.choo@ntu.edu.sg

	cell programming) will become key to the success of the regenerative medicine and cell therapy industry. Programming of cells using lineage control networks has the potential to transform how we make cell therapies and immunotherapies, develop regenerative medicines, and create cellular models for research. However, identifying specific combinations of master regulatory genes known as transcription factors (TFs) that lead to highly efficient conversion of a scalable starting cell (e.g. iPSC, fibroblast) into desired cell types for biomedical applications (e.g. T cell, b cell) remains a significant challenge and a longstanding, critical bottleneck in the field. In this programme we will use an innovative combinatorial screening technology to rapidly assess the effectiveness of thousands of combinations of TFs in programming various human cell types into specific lineages that enable high value biomedical applications. Cell types we may derive in this project have diverse applications, including in: 1) developing advanced cellular/tissue models for biomedical R&D, 2) cGMP manufacturing of cell and gene therapies, including allogeneic immunotherapies, and 3) in vivo reprogramming for regenerative medicine and autologous immunotherapies.	
	6. **Data Science**	
6.1	**Deep learning for Robust Analysis of Medical Scans** The doctoral project aims to develop a deep learning system for automated analysis of medical imaging scans such as X-rays, CT, and MR scans. The system will utilise deep learning models trained on large datasets of scans for different medical tasks. Students can conduct research on medical deep learning projects which includes: • Object detection in medical scans • Computer vision for medicine and population health	**Asst Prof Yeo Si Yong** **siyong.yeo@ntu.edu.sg** **Website** https://medvisailab.github.io/research/

	• Medical segmentation, diffusion, reconstruction, and classification • Deep learning for the analysis of multi-modal medical dataset • Large language models for the analysis of medical imaging dataset • Large foundation models for medicine	
6.2	**Systematically Investigating Molecular Mechanisms Underlying Aging-Related Human Diseases through Multi-Omics Profiling** Aging is a complex biological process characterized by a gradual decline in physiological functions, which increases susceptibility to diseases and death. This process is influenced by a myriad of genetic, environmental, and lifestyle factors. To better understand aging and study the relationship between aging and aging-related diseases, our research group is focused on building predictive models using machine learning techniques. The model is to integrate multi-omics datasets, focusing specifically on gut microbiome and metabolomics data. The comprehensive analysis of these multi-omic datasets aims to unveil crucial molecular indicators, intricate biological pathways, and influential regulatory circuits that play a role in the aging process and the pathogenesis of age-associated disorders. Such an understanding is likely to be helpful in the development of innovative therapeutic interventions to promote healthy aging and to address the onset and progression of neurodegenerative conditions such as Alzheimer's and Parkinson's diseases.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
6.3	**Comprehensive Multi-omics Analysis of Human Aging Using the Large Language Module based Functional Module Annotation** Multi-omic methods provide great opportunities to systematically reveal the critical molecular alterations of aging from a multidimensional perspective, while matching and investigating the biological information and functions from multi could be a heavy subjective	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)

	work. Large Language Models (LLMs) has shown high efficiency and accuracy in repetitive search and collection work, which will help us to extensively and quickly investigate potential research objects and validate them with published works to prove their roles and molecular mechanism. So in this project, we aim to build up a tool utilizing LLM, such as GPT4, to accelerate and improve the biological investigation in multi-omics data for aging research.	
6.4	**Data-driven Approaches for Mitigating Climate-related Health Risks** As climate change and extreme weather events become more frequent worldwide, understanding their impact on public health is crucial. This research aims to investigate the relationship between climate-induced hazards and health outcomes. A key example is the 2022 malaria outbreak in Pakistan, the worst in 50 years. This outbreak followed severe flooding that damaged homes, infrastructure, and crops. Using comprehensive data, advanced statistical modelling, and simulations, we will explore the connections between hazard intensity, conducive environmental conditions (for example, for mosquito breeding), and the incidence of disease. By linking these factors to health outcomes in the population and healthcare facilities, our findings will provide valuable insights for emergency management and hospital resource planning.	**Dr Michele Nguyen** michele.nguyen@ntu.edu.sg **Website** www.drmichelenguyen.com
6.5	**Healthcare extremes: forecasting and characterisation** Extreme events are present in every level of the health system: from adverse clinical outcomes in patients, to disease outbreaks. Since extreme events are by nature rare, we have less data on them than common, day-to-day occurrences. Traditional statistical methods fall short due to this unbalanced data. This project focuses on developing methods from for example, extreme value (EV) analysis, to characterise, forecast and manage rare heath system events. We will investigate ways to enhance existing EV models and allow for the changing nature of “extremes” in the context of climate change and societal adaptation. The findings have implications for resource planning and	**Dr Michele Nguyen** michele.nguyen@ntu.edu.sg **Website** www.drmichelenguyen.com

	health early warning systems, and contribute towards increasing resilience against extreme health events.	
6.6	**Discovery of Gut Microbiome-Metabolized Bioactive Compounds from Traditional Chinese Medicine** We propose to culture human gut microbiomes with Traditional Chinese Medicine (TCM) extracts and apply a novel computational algorithm to identify new bioactive compounds metabolized by the microbiota. This integrative platform enables systematic discovery of microbiome-derived metabolites from natural products, uncovering mechanisms underlying TCM efficacy and revealing potential therapeutic agents. Beyond discovery, we aim to construct a comprehensive atlas of gut microbiome-metabolized TCM and natural products. This resource will serve as a foundation for drug development and precision therapeutics based on host–microbe–metabolite interactions.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
6.7	**Explaining Medical Imaging with Clinically Meaningful Explanations with XAI** This PhD project, titled **"Explaining Medical Imaging with Clinically Meaningful Explanations with XAI,"** aims to bridge the gap between artificial intelligence (AI) in medical imaging and clinical practice by developing advanced explainable AI (XAI) techniques that provide interpretations directly aligned with clinical understanding. The project will focus on designing XAI models that generate explanations using clinically meaningful concepts, such as anatomical features, pathology characteristics, and diagnostic criteria, making the explanations transparent and actionable for clinicians. Methods will include feature attribution, concept-based explanations, and multimodal fusion to enhance interpretability. The project targets applications in radiology, dermatology, and ophthalmology.	**Asst Prof Fan Xiuyi** xyfan@ntu.edu.sg
6.8	**Irregular Time Series in Medical AI** This PhD project, titled **"Irregular Time Series in Medical AI,"** focuses on developing advanced machine learning models capable of handling irregular time series data, a common challenge in medical settings. Irregular time series occur when data points	**Asst Prof Fan Xiuyi** xyfan@ntu.edu.sg

	are collected at inconsistent intervals, such as patient vital signs recorded at varying times or sporadic medical test results. The project aims to design novel algorithms that can effectively learn from such data, leveraging techniques like temporal interpolation, attention mechanisms, and neural differential equations. These methods will be applied to medical domains, including patient monitoring, disease progression prediction, and personalized treatment planning.	
6.9	**Metabolic feature-based functional module analysis based on the large language model** We propose to develop featureFMA, a novel large language model (LLM)-guided computational framework for metabolic feature-based functional module analysis in LC-MS untargeted metabolomics. Traditional pathway analysis lacks specificity and coverage for metabolomics data. featureFMA will integrate metabolite annotation, metabolic network modeling, and LLM-based functional interpretation to identify dysregulated modules linked to biological functions and diseases. This project includes software development (R package, Shiny app, and cloud platform), multi-species validation, and diverse case studies (e.g., enzyme mutation and gut microbiome). featureFMA will provide a scalable, intelligent solution for interpreting complex metabolomics data and accelerating functional discovery in systems biology.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
6.10	**Sustainable Precision Healthcare: Predictive Modelling and Global Strategies for Environmentally Linked Diseases** ***Remarks: Project may be supported by scholarship funding*** Precision healthcare promises to transform disease prevention, diagnosis, treatment and prognosis by tailoring interventions to individual risk profiles. However, its adoption faces challenges of cost, feasibility, and contextual relevance. This research addresses these gaps by: (1) developing and evaluating predictive modelling frameworks for environmentally dependent diseases including respiratory illnesses; (2) quantifying the incremental predictive and clinical value of biomarkers, molecular signatures, phenotypes, endotypes, and external	**Dr Michele Nguyen** michele.nguyen@ntu.edu.sg **Website** www.drmichelenguyen.com **Co-Supervisor:** Assoc Prof Sanjay Chotirmall Asst Prof Liang Yao

	determinants including environmental exposures and socio-economic risks; and (3) assessing implementation feasibility and implications across high-income and low- and middle-income countries. The findings will provide evidence to guide equitable and sustainable precision healthcare strategies globally.	
6.11	**The "Burden of Evidence" in Respiratory and Infectious Medicine: Quantifying the Impact of Low-Quality Research on Health Equity and AI Integrity** ***Remarks: Project may be supported by scholarship funding*** The annual output of MEDLINE-indexed articles now exceeds one million, creating a paradox where more information often leads to less clarity. Medical knowledge increasingly reaches clinicians through fragmented feeds designed for engagement rather than accuracy. This phenomenon has created a "burden of evidence." Analogous to the "burden of disease," this concept measures the systemic prevalence of low-quality, biased, and redundant research. This burden is not merely a waste of resources; it is an active pollutant in the healthcare ecosystem that distorts clinical guidelines, threatens health equity, and poisons the datasets used to train the next generation of medical Artificial Intelligence (AI). To address this, we must shift from celebrating research volume to interrogating its integrity. This PhD project aims to quantify and characterize the burden of evidence specifically within Respiratory and Infectious Diseases—a field critically impacted by rapid, high-volume publication cycles. The research will proceed in two objectives: (1) Primary Research Assessment: Systematically evaluate the prevalence of "high risk of bias" in pivotal randomized controlled trials and observational studies within the field. (2) Synthesis quality qssessment: Determine the proportion of evidence summaries (systematic reviews and meta-analyses) that are proved as low-certainty evidence to form conclusions. (3) Impact and uptake analysis: Trace the downstream penetration of this low-quality evidence by quantifying how frequently these flawed studies are cited in major clinical guidelines and policy documents. By mapping the extent of this "evidence burden" this project will provide a framework to decontaminate clinical decision-making and ensure	**Dr Liang Yao** Liang.yao@ntu.edu.sg **Website** https://www.liamyao.com/ **Co-Supervisor:** Asst Prof Michele Nguyen Assoc Prof Sanjay Chotirmall

	that future health policies and AI tools are built upon a foundation of trustworthy data.	
	7. **Cancer Discovery & Regenerative Medicine**	
7.1	**Cardio-immunology: Elucidating the immune landscape of transplanted human cardiovascular progenitors in myocardial infarcted hearts** Ischemic heart failure is a non-communicable disease that affects a large number of individuals globally. A potential treatment that may enhance heart function and functionally replace injured cardiac muscles in cellular therapy. However, there is a gap in knowledge in understanding the immune rejection of xenograft after transplantation into myocardial infarcted hearts. Having this knowledge will be essential to devise strategies to target immune responses for a successful regenerative medicine therapy.	**Asst Prof Lynn Yap** lynn.yap@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp02163 https://www.linkedin.com/in/lynn-yap-39969879/
7.2	**The role of microtrauma in human hair regrowth and regeneration** Androgenetic alopecia (or male pattern baldness) affects more than half of men by the time they reach middle age, whereby hair follicles miniaturise over time. We currently do not understand the mechanism of the human hair cycle, or how to reverse miniaturization. The popularity of treatments like microneedling suggest that subclinical wounding (ie. Microtrauma) has a role in allowing hair follicle stem cells and their microenvironment to regenerate. Our team is focused on understanding the basic mechanisms of microtrauma on human skin and hair follicles, and translating these findings into exciting new treatments for hair loss.	**Co-Supervisor:** **Asst Prof Etienne Wang** etienne@nsc.com.sg

7.3	**Generating immune-privileged kidney organoids from gene-edited human pluripotent stem cells** Autologous induced pluripotent stem cell (iPSC) derived cells and tissues represent a valuable resource for realizing disease modelling and replacement. However, it is time-consuming and costly to generate fully characterised GMP grade iPSCs from every patient who requires organ replacement therapy. In this project, we will harness gene editing to generate human iPSCs the progenies of which can evade T cells, NK cells, and complement system of immune competent rodent host.	**Asst Prof XIA Yun** yunxia@ntu.edu.sg **Website**
7.4	**In-vivo functional genetic screen to identify novel modulators of Non-Alcoholic Fatty Liver Disease (NAFLD)** The project focuses on employing in-vivo mouse models that resemble and recapitulate human disease to study NAFLD disease progression. Our preliminary results have identified several shRNAs that confer a negative or positive effect on the regenerative capacity of the hepatocytes. Further approach will be focused on validation of these shRNAs, such as their cell migration and cell proliferation characteristics using various in-vitro assays, followed by selection of the top performing shRNAs for in-vivo validation. In addition, combined transcriptomic and proteomic approaches will be undertaken to unravel new insights with the aim of identifying targets for therapeutic intervention and treatment of the disease.	**Assoc Prof Torsten Wuestefeld** Torsten.Wuestefeld@ntu.edu.sg
7.5	**Identification of novel senolytic targets for improving liver regeneration** The project focuses on conducting in vivo & in vitro functional genetic screens to identify targets to eliminate senescent cells. Senescent cells are known to drive inflammaging attenuating the regenerative capacity of the liver. Through a negative selection screen in senescent cells we can identify vulnerabilities	**Assoc Prof Torsten Wuestefeld** Torsten.Wuestefeld@ntu.edu.sg

	of these cells. The goal is to identify novel senolytic targets for therapeutic purposes.	
7.6	**Identifying novel biomarkers in liquid biopsy derived exosomes** The project focuses on identifying novel blood-based biomarkers for liver disease. Mouse models of chronic liver disease will be used, exosomes will be isolated from the blood and the content will be analyzed by transcriptomic and proteomic approaches. The same approach will be applied for liver patient derived blood samples. The goal is to identify novel conserved biomarkers for liver disease.	**Assoc Prof Torsten Wuestefeld** Torsten.Wuestefeld@ntu.edu.sg
7.7	**Countering Cancer's Therapeutic Resistance Using Synthetic Lethality CRISPR Screen** Therapeutic resistance is one of the major causes of treatment failure and poor prognosis in cancer. With the advent of CRISPR screen technology, we are now able to identify the novel genetic weaknesses of cancers that developed resistance to conventional treatments such as chemo-/radio-therapy and targeted therapy. To identify and specifically target the 'Achilles' heels' of these obstinate cancers, the PhD candidate will perform state-of-the-art in vitro and/or in vivo CRISPR screens followed by validation and mechanistic studies. Upon successful validation of the screen hits and the elucidation of the underlined mechanism, the candidate will test the findings in animal model or patient derived xenograft/ organoid models to provide pre-clinical insights that could potentially guide clinical practice. Other than identifying novel genetic dependences (weaknesses) from scratch, the PhD candidate can also choose to work on countering already identified genetic dependences in obstinate cancer. In this case, developing therapeutic strategies countering these weaknesses will become the overarching objective of the PhD thesis. The candidate will be testing out this possibility by re-purposing the FDA approved medications or exploiting various drug development strategies including but not limited to in silico drug/	**Asst Prof Hongbin Yang** Hongbin.yang@ntu.edu.sg

	natural product screen, antisense oligonucleotide (ASO) design, AI facilitated peptide/ peptidomimetics design, and proteolysis-targeting chimera (PROTAC) development.	
7.8	**Identifying Key Determinants and Regulators of Metastasis Using in vivo CRISPR Screen** Cancer-related deaths are partly due to distant metastases and our current inability to eliminate them. Therefore, one possible approach to reduce cancer death is to target the key factor(s) required for metastasis so as to restrain tumour cells to their primary site for surgical removal. For already metastasized tumour, it is also possible to restrain further progression if weaknesses of metastatic cancer cells are identified and therapeutically targeted. Increasing evidence showed that metastasis is a combinational outcome of not only cancer cells' own efforts but also the facilitations from the non-cancerous cells in the microenvironment. The currently reported CRISPR screens aiming to identify metastasis-mediating factors were all in vitro, therefore, fell short of recapitulating such tumour-microenvironment interaction. The PhD candidate will have the opportunity to optimize and conduct a novel in vivo CRISPR screen specifically designed to identify key determinants and regulators of metastasis. This in vivo screen will not only potentiate the cancer-microenvironment crosstalk, but also provide all realistic routes, destinations, and challenges for metastatic process at organismal level. Upon successful validation of the screen hits and the elucidation of the underlined mechanism, the candidate will test the findings in animal model or patient derived xenograft/ organoid models to provide implications for treatment development.	**Asst Prof Hongbin Yang** Hongbin.yang@ntu.edu.sg
7.9	**Ageing of bone microenvironments** Our skeletons play a crucial role in regulating key physiological processes, including mineral homeostasis, energy metabolism, and blood cell production. The presence of multiple blood vessel (BV)	**Assoc Prof Saravana Kumar Ramasamy** saravana.kr@ntu.edu.sg

	subtypes and the distinct microenvironments they support contribute to the skeleton's multifaceted functions. Vascular aging is a key factor in the age-related functional and physical changes observed in the skeleton. Understanding vascular niches and their age-related alterations could help target specific functional niches for managing age-related bone and blood diseases. In this study, we aim to identify and characterize bone vascular microenvironments and their functions. Leveraging cutting-edge techniques developed in our laboratory—including high-resolution 3D imaging, single-cell and spatial transcriptomics, metabolic analysis, and advanced mouse genetics—the candidate will have the opportunity to: • Characterize different types of microenvironments in bone. • Understand how blood vessels support these niches. • Identify strategies to replace or target aging blood vessel subtypes specifically.	
7.10	**Metabolic control of bone marrow microenvironments** The mammalian skeletal system undergoes continuous remodelling throughout life, intricately interacting with whole-body physiology. Metabolic changes significantly influence bone health by altering the cellular composition and functional dynamics of bone tissue. However, the cellular and molecular mechanisms underlying these dynamic changes remain poorly understood. In this study, we investigate the impact of metabolism on the mesenchymal composition of bone microenvironments. Specifically, the student will 1. Map and characterize the distribution patterns of mesenchymal cell subtypes in bone. 2. Explore how metabolic conditions such as diabetes, modulate mesenchymal cell composition	**Assoc Prof Saravana Kumar Ramasamy** saravana.kr@ntu.edu.sg

	3. Identify metabolic targets to modulate mesenchymal cell differentiation and composition. The student will employ advanced techniques, including confocal and intravital imaging, single-cell and spatial transcriptomics, metabolic profiling, and state-of-the-art mouse transgenics. Overall, this study aims to uncover the mechanisms driving bone pathology in metabolic diseases like diabetes, providing a foundation for targeted therapeutic strategies.	
7.11	**Understanding the tumor microenvironment: High-resolution 3D and multiplex imaging approach for deciphering cancer progression** Endothelial cells are pivotal architects of blood and lymphatic vessel integrity, forming the inner lining that regulates inflammation, immune cell trafficking, and organ-specific vascular functions. Perivascular and mesenchymal stromal cells dynamically shape vascular microenvironments, playing essential roles in tissue homeostasis and disease. In cancer, the tumor microenvironment (TME) drives disease progression by orchestrating a complex interplay among cancer cells, vascular networks, and stromal components. This dynamic milieu enhances metastatic potential and contributes to therapeutic resistance. Central to this process is epithelial-mesenchymal transition (EMT), which equips cancer cells with invasive properties. Critically, stromal and vascular cells are key enablers of EMT and therapy resistance, making them highly attractive targets for innovative therapeutic strategies. Despite their significance, the complexity, heterogeneity, and spatial interactions of tumor stroma and vasculature remain poorly understood across different stages of cancer progression. This knowledge gap limits the development of precision therapies. To address this challenge, we propose leveraging cutting-edge high-resolution light-sheet microscopy and multiplex imaging to define, at an unprecedented level, the spatial interactions between vascular, stromal, and cancer cells throughout disease progression. Our approach focuses on three malignancies with distinct	**Assoc Prof Anjali Parmanand Kusumbe** anjali.pkusumbe@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp02539

	clinical and biological challenges: head and neck cancers, glioblastoma, and breast tumors. This study aims to illuminate the spatial interactions within the TME, providing a foundation not only for the development of targeted interventions to disrupt the stromal-vascular axis in cancer progression but also for precise diagnostic and prognostic strategies throughout the course of the disease.	
7.12	**Modeling Tertiary Lymphoid Structures in Solid Tumors: Unveiling Immune Modulation and Therapeutic Potential** This PhD project aims to model tertiary lymphoid structures (TLS) in solid tumors to investigate their influence on the tumor microenvironment and response to cancer therapy. Using advanced in vitro techniques, the project will create a robust model system that mimics TLS formation, allowing us to explore interactions between immune cells and tumor cells. The student will gain experience with cutting-edge technologies in immunology and cancer biology and contribute to crucial discoveries in the tumor immune landscape. This research will offer new insights into TLS functions in cancer, with potential applications in developing more effective cancer treatments.	**Asst Prof Andrea Pavesi** Andrea.pavesi@ntu.edu.sg www.pavesilab.com
7.13	**Modeling Tumor-Immune Interactions in Glioblastoma** Join our lab to develop an advanced glioblastoma (GBM) model that integrates the blood-brain barrier and immune components to better understand tumor-immune interactions. This PhD project focuses on investigating the role of tertiary lymphoid structures (TLS) within the GBM microenvironment and exploring immunotherapy strategies targeting both GBM and TLS. This interdisciplinary project offers hands-on experience in cutting-edge cancer biology techniques, advanced model development, and preclinical testing—ideal for students passionate about driving	**Asst Prof Andrea Pavesi** Andrea.pavesi@ntu.edu.sg www.pavesilab.com

	innovation in cancer immunotherapy and tumor microenvironment research.	
7.13	**Defining the roles of spindle dynamics in pluripotent stem cell fate decisions** A fundamental question in developmental biology is how cells interpret intrinsic and extrinsic cues to make fate decisions. While the roles of transcription factors and niche-derived signals are well characterized, recent work has identified the mitotic spindle as an unexpected mechanical regulator of cell fate, coupling cytokinesis with transcriptional reprogramming in adult systems[1–5]. However, in early embryogenesis—where a homogeneous population of pluripotent stem cells must generate heterogeneity and undergo symmetry breaking—the mechanisms initiating these processes remain poorly understood. This PhD project will test the hypothesis that the mitotic spindle acts as an intracellular mechanical orchestrator of fate specification during early development. Specifically, whether the spindle-dependent processes integrate intracellular biochemical cues (e.g., intracellular pH dynamics) with intercellular communication (e.g., cytoplasmic bridges) to drive fate diversification. By dissecting this link between mechanics and biochemistry, this work could redefine paradigms of cell fate determination, with broader implications for regenerative medicine and cancer biology—where aberrant spindle mechanics and pH dysregulation are hallmarks of disease progression.	**Asst Prof Yi Liu** yi.liu@ntu.edu.sg **Website** https://liulab.myportfolio.com/
7.14	**Decoding the intracellular pH-sensing pathway that specifies regenerative intestinal stem cells** Stem cell-mediated regeneration is essential for tissue repair, and understanding this process is critical for advancing regenerative medicine. In the intestinal epithelium, regeneration following injury is driven by Clusterin-positive (Clu^+) stem cells[6], which remain quiescent under homeostasis but activate upon damage. Despite their therapeutic potential, the	**Asst Prof Yi Liu** yi.liu@ntu.edu.sg **Website** https://liulab.myportfolio.com/

	regulatory mechanisms controlling Clu^+ stem cell fate specification remain poorly understood. Our previous work demonstrated that decreasing intracellular pH (pHi) expands the Clu^+ cell population and that pHi-dependent Clu expression inversely correlates with reduced expression of AP-1 components, suggesting a regulatory crosstalk, and highlighting decreasing pHi as a non-invasive approach to elicit a regeneration response. Given that AP-1 integrates multiple differentiation signals and is modulated by PARP1-mediated ADP-ribosylation, this PhD project will test the hypothesis that PARP1-AP-1-CLU is a cytosolic pathway mediating pHi-dependent stem cell differentiation. This project will define the mechanistic connections between PARP1, AP-1, and Clu^+ stem cell behavior, leveraging genetic, biochemical, and cell biology approaches in physiologically relevant human intestinal organoids as well as *in vivo* animal models. By resolving this novel model wherein, the PARP1-AP-1-CLU axis transduces pHi signals to orchestrate stem cell differentiation during regeneration, it will not only advance fundamental understanding of pHi-regulated stem cell fate decisions but also provide actionable insights for enhancing regenerative therapies. References 1. Zhong, T. & Zhou, J. Orientation of the Mitotic Spindle in the Development of Tubular Organs. *J of Cellular Biochemistry* **118**, 1630–1633 (2017). 2. Snippert, H. J. *et al.* Intestinal Crypt Homeostasis Results from Neutral Competition between Symmetrically Dividing Lgr5 Stem Cells. *Cell* **143**, 134–144 (2010). 3. Hu, D. J.-K. & Jasper, H. Control of Intestinal Cell Fate by Dynamic Mitotic Spindle Repositioning Influences Epithelial Homeostasis and Longevity. *Cell Reports* **28**, 2807-2823.e5 (2019). 4. Sei, Y., Feng, J., Chow, C. C. & Wank, S. A. Asymmetric cell division-dominant neutral drift model for normal intestinal stem cell homeostasis. *American Journal of Physiology-Gastrointestinal and Liver Physiology* **316**, G64–G74 (2019). 5. Bellaïche, Y., Gho, M., Kaltschmidt, J. A., Brand, A. H. & Schweisguth, F. Frizzled regulates localization of cell-fate determinants and mitotic spindle rotation during asymmetric cell division. *Nat Cell Biol* **3**, 50–57 (2001).	

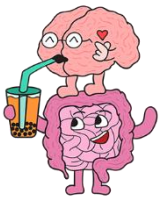
	6. Ayyaz, A. *et al.* Single-cell transcriptomes of the regenerating intestine reveal a revival stem cell. *Nature* **569**, 121–125 (2019).	
7.15	**Bat-inspired targets to fight human diseases and aging** The objective is to learn from bats with exceptional disease resistance and healthy longevity, aiming to translate these lessons into new targets to fight human diseases and extend healthspan. The pioneering work in bat inflammation (*Nat Micro* 2019, *PNAS* 2020, *Nature* 2021, *Cell* 2023 and ongoing development of a new class of anti-inflammatory drugs) has helped establish bats as a great model to uncover new strategies to fight human diseases and has just scratched the surface of what we can learn from bats to benefit humans. The three different and synergistic approaches include 1) 'unbiased' multi-omics aging atlas of bats 2) 'disease centric' disease-free bat models including metabolic and neurological diseases and 3) 'more targeted' study of enhanced proliferation/regeneration and increased apoptosis as potential anti-aging/cancer mechanisms.	**Asst Prof Ahn Matae** matae.ahn@ntu.edu.sg https://dr.ntu.edu.sg/entities/person/Matae-Ahn
7.16	**Direct cell reprogramming for biomedical applications** ***Remarks: Project may be supported by scholarship funding*** The manufacture of advanced stem cell-based products and therapies through directed differentiation faces significant challenges in achieving efficient, reliable, and scalable production of specialized cell types especially in a cGMP setting. Cell differentiation approaches involve stepwise culture of (pluripotent) stem cells to direct their development into target cell types. However, current manufacturing methods are generally not fit for purpose - being often hampered by complex, lengthy and costly protocols, low cell yield, purity and/or quality, and inconsistent outcomes - limiting industrial applications. Direct (or forward) cell programming offers a promising alternative by enabling the direct conversion of one cell type into another by activating gene	**Associate Prof Yen CHOO** yen.choo@ntu.edu.sg

	regulatory networks that determine cell identity. This approach has the potential greatly to streamline the manufacturing process, reduce the time and resources required, and improve the consistency and functionality of cellular products. As the advanced therapy field develops, establishing robust, scalable manufacturing technology platforms (such as by direct cell programming) will become key to the success of the regenerative medicine and cell therapy industry. Programming of cells using lineage control networks has the potential to transform how we make cell therapies and immunotherapies, develop regenerative medicines, and create cellular models for research. However, identifying specific combinations of master regulatory genes known as transcription factors (TFs) that lead to highly efficient conversion of a scalable starting cell (e.g. iPSC, fibroblast) into desired cell types for biomedical applications (e.g. T cell, b cell) remains a significant challenge and a longstanding, critical bottleneck in the field. In this programme we will use an innovative combinatorial screening technology to rapidly assess the effectiveness of thousands of combinations of TFs in programming various human cell types into specific lineages that enable high value biomedical applications. Cell types we may derive in this project have diverse applications, including in: 1) developing advanced cellular/tissue models for biomedical R&D, 2) cGMP manufacturing of cell and gene therapies, including allogeneic immunotherapies, and 3) in vivo reprogramming for regenerative medicine and autologous immunotherapies.	
8. **Microbiome Medicine**		
8.1	**Investigating the role of gut microbiome in cardiometabolic diseases** In recent years, it has become evident that the gut bacteria living in our intestine significantly impact health and disease. This influence extends beyond intestinal disorders like inflammatory bowel disease to encompass a wide range of conditions including	**Asst Prof Kazuyuki Kasahara** kazuyuki.kasahara@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp02039 https://kasaharalab.com

	obesity, diabetes, and neurodegenerative diseases. Our laboratory has previously reported that certain gut bacteria contributes to the progression of cardiovascular disease (PMID: 30397344, 37279756). This PhD project focuses on gut microbiota and lipid metabolism, employing state-of-the-art technologies such as anaerobic culture systems, mouse models, and next-generation sequencing to advance research in this field.	
8.2	**Systematically Investigating Molecular Mechanisms Underlying Aging-Related Human Diseases through Multi-Omics Profiling** Aging is a complex biological process characterized by a gradual decline in physiological functions, which increases susceptibility to diseases and death. This process is influenced by a myriad of genetic, environmental, and lifestyle factors. To better understand aging and study the relationship between aging and aging-related diseases, our research group is focused on building predictive models using machine learning techniques. The model is to integrate multi-omics datasets, focusing specifically on gut microbiome and metabolomics data. The comprehensive analysis of these multi-omic datasets aims to unveil crucial molecular indicators, intricate biological pathways, and influential regulatory circuits that play a role in the aging process and the pathogenesis of age-associated disorders. Such an understanding is likely to be helpful in the development of innovative therapeutic interventions to promote healthy aging and to address the onset and progression of neurodegenerative conditions such as Alzheimer's and Parkinson's diseases.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
8.3	**Comprehensive Multi-omics Analysis of Human Aging Using the Large Language Module based Functional Module Annotation**	**Asst Prof Shen Xiaotao**

	Multi-omic methods provide great opportunities to systematically reveal the critical molecular alterations of aging from a multidimensional perspective, while matching and investigating the biological information and functions from multi could be a heavy subjective work. Large Language Models (LLMs) has shown high efficiency and accuracy in repetitive search and collection work, which will help us to extensively and quickly investigate potential research objects and validate them with published works to prove their roles and molecular mechanism. So in this project, we aim to build up a tool utilizing LLM, such as GPT4, to accelerate and improve the biological investigation in multi-omics data for aging research.	xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
8.4	**Gut Microbiome Signatures in Colorectal Cancer Molecular Subtypes and Tumour Metabolism** This project will investigate the role of the gut microbiome in modulating molecular subtypes and tumour metabolism in colorectal cancer. Recent studies have highlighted the importance of the gut microbiome in influencing cancer development and progression. This project aims to elucidate the specific microbial signatures and metabolic pathways associated with different molecular subtypes of colorectal tumours. The findings could lead to the development of microbiome-based biomarkers and therapeutic strategies targeting the tumour microenvironment.	**Assoc Prof Sunny Wong** sunny.wong@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp01651
8.5	**Exploring Gastrointestinal Interoception, Microbiome, and Nutrients in Disorders of Gut-Brain** This project will explore the gut-brain axis and its role in various neurological and psychiatric disorders. The study will investigate the mechanisms underlying gastrointestinal interoception, the microbiome-gut-brain signalling, and the influence of nutrition on these pathways. By understanding the complex interplay between the gut and the brain, the project aims to	**Assoc Prof Sunny Wong** sunny.wong@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp01651

	provide insights into the pathogenesis of gut-brain disorders and identify potential therapeutic targets.	
8.6	**Gut Microbiome Dysbiosis and Its Role in Metabolic-Associated Cancers** This project will investigate the interplay between the gut microbiome, metabolic disorders, and the development of metabolic-associated cancers. Emerging evidence suggests that dysbiosis of the gut microbial community can contribute to the pathogenesis of obesity, type 2 diabetes, and related metabolic conditions, which are known risk factors for certain types of cancer. The study aims to elucidate the specific microbial signatures, metabolic pathways, and inflammatory mechanisms that link gut microbiome alterations to the initiation and progression of metabolic-associated cancers, such as hepatocellular carcinoma and endometrial cancer. The findings could inform the development of microbiome-based diagnostic and therapeutic strategies.	**Assoc Prof Sunny Wong** sunny.wong@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp01651
8.7	**Gut Microbiome, Dietary Patterns, and Metabolic Health in a Multi-Ethnic Asian Population: A Singapore-Based Study** Singapore is a highly urbanised and multiethnic country in Southeast Asia, with a diverse population comprising primarily Chinese, Malay, and Indian ethnic groups. Dietary patterns and food cultures vary significantly across these ethnic communities, which may influence the gut microbiome and overall health outcomes. This project aims to investigate the complex interplay between the gut microbiome, dietary habits, and nutritional status in the Singaporean population. The findings can inform the development of culturally-relevant nutritional interventions and microbiome-based strategies to address public health challenges in Singapore and similar urban, multiethnic settings.	**Assoc Prof Sunny Wong** sunny.wong@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp01651
8.8	**Modulation of digestive enzyme activity as a safe approach to improve metabolism and health**	**Assoc Prof Yusuf Ali** Yusuf.ali@ntu.edu.sg

	This project aims to design new therapeutic targets, with structure-function lead optimisation of compounds that inhibit luminal carbohydrate enzymes. Guided by naturally occurring plant-based compounds, this project involves side-chain modifications to improve enzyme inhibition selectivity and specificity. From chemistry to biology, this project will continue with the characterization of luminal carbohydrate digestion modulation on the recipient host. Investigations will include an assessment of intestinal health, alterations in gut microbiome, impact on immunology and finally carbohydrate metabolism and homeostasis.	**Website** https://dr.ntu.edu.sg/cris/rp/rp00609 **Assoc Prof Zaher Judeh** **(Co-sup)**
8.9	**Gut-brain neurobiology: microbiome control of neural circuits and behaviour** The trillions of bacteria living in our body encode over 46 million genes – suggesting tremendous functional capacity (by contrast, the human genome has less than a thousandth of that). Moreover, emerging evidence suggests that the gut microbiota profoundly influences host physiology and behaviour. In this project, we will investigate the fundamental biological basis of "gut-feelings", how microorganisms and chemicals in the gut signal to brain to modulate neural substrates that control physiology and behaviour. We employ a range of experimental techniques in mice to study the mammalian gut-brain axis including sequencing, metabolomics, in vivo neural imaging/recording, and genetically-guided functional interrogation.	**Asst Prof Hwei-Ee TAN** hweiee.tan@ntu.edu.sg **Website** tanlab.science 
8.10	**Deciphering the Role of Atypical LPS and MAMPs in Gut Barrier Dysfunction and MASLD** The gut barrier is a critical defense system, preventing harmful microbes and toxins from entering circulation while supporting a balanced relationship with gut bacteria. When this barrier is compromised, it contributes to a cascade of chronic diseases. One of the most pressing concerns is Metabolic-Associated Steatotic Liver Disease (MASLD), a leading cause of chronic liver disease worldwide, which is increasingly linked to gut microbial imbalances. This PhD project will explore how microbe-associated molecular	**Assoc Prof Andrew Tan Nguan Soon** nstan@ntu.edu.sg https://dr.ntu.edu.sg/cris/rp/rp00393

	patterns (MAMPs), specifically classical and atypical lipopolysaccharides (LPS), influence gut barrier integrity via Angiopoietin-like protein 4 (Angptl4), a key regulator of lipid metabolism and inflammation. However, the precise molecular mechanisms by which these LPSs regulate Angptl4 remain unknown. Using cutting-edge microbiome analysis, biochemical characterization, and in vivo models, you will uncover how microbial signals shape gut-liver communication. The candidate will analyze bacterial LPS, assess receptor activation and gut permeability, and utilize germ-free mouse models. **Why Join This Project?** You'll gain expertise in host-microbe interactions, molecular biology, and immunology, with opportunities for clinical collaborations. **Who Should Apply?** We welcome applications from motivated candidates with a background in microbiology, molecular biology, immunology, bioinformatics, or a related field. A passion for host-microbe interactions and translational medicine is essential. Join us in uncovering how the gut microbiome influences metabolic disease and paving the way for microbiome-based therapeutics! References: Low, ZS, Chua, D., Cheng, H.S. et. al (2024). The LIDPAD Mouse Model Captures the Multisystem Interactions and Extrahepatic Complications in MASLD. **Adv. Sci.** 11(35): e2404326.	
8.11	**Discovery of Gut Microbiome-Metabolized Bioactive Compounds from Traditional Chinese Medicine** We propose to culture human gut microbiomes with Traditional Chinese Medicine (TCM) extracts and apply a novel computational algorithm to identify new bioactive compounds metabolized by the microbiota. This integrative platform enables systematic discovery of microbiome-derived metabolites from natural products, uncovering mechanisms underlying TCM efficacy and revealing potential therapeutic agents. Beyond discovery, we aim to construct a comprehensive atlas of gut microbiome-metabolized TCM and natural products. This resource will serve as a foundation for drug development and precision therapeutics based on host–microbe–metabolite interactions.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)

8.12	**Metabolic feature-based functional module analysis based on the large language model** We propose to develop featureFMA, a novel large language model (LLM)-guided computational framework for metabolic feature-based functional module analysis in LC-MS untargeted metabolomics. Traditional pathway analysis lacks specificity and coverage for metabolomics data. featureFMA will integrate metabolite annotation, metabolic network modeling, and LLM-based functional interpretation to identify dysregulated modules linked to biological functions and diseases. This project includes software development (R package, Shiny app, and cloud platform), multi-species validation, and diverse case studies (e.g., enzyme mutation and gut microbiome). featureFMA will provide a scalable, intelligent solution for interpreting complex metabolomics data and accelerating functional discovery in systems biology.	**Asst Prof Shen Xiaotao** xiaotao.shen@ntu.edu.sg **Website** Shen Lab (shen-lab.org)
9. **Medical Education**		
9.1	**Climate and health – mapping the impacts towards positive action** This PhD is located within a wider multidisciplinary project NTU “Climate Transformation Program” that seeks to map and model impacts of climate change. World Health Organization (WHO) emphatically noted that the risks of the climate crisis to human health extend way beyond physical impact(s) to mental health and called for intervention(s), mitigation and adaptation. The evidence however on mental health impacts in Singapore and Southeast Asia is limited. The PHD project will integrate evidence synthesis and observational mixed methods approached to identify mental health risks and at risk populations.	**Assoc Prof Konstadina Griva** Konstadina.griva@ntu.edu.sg https://earthobservatory.sg/research/climate climate-transformation-programme **Co-supervisor:** **A/P Steve Yim**
10. **Others**		

10.1	**Chemistry and Bioengineering** **Modulation of digestive enzyme activity as a safe approach to improve metabolism and health** This project aims to design new therapeutic targets, with structure-function lead optimisation of compounds that inhibit luminal carbohydrate enzymes. Guided by naturally occurring plant-based compounds, this project involves side-chain modifications to improve enzyme inhibition selectivity and specificity. From chemistry to biology, this project will continue with the characterization of luminal carbohydrate digestion modulation on the recipient host. Investigations will include an assessment of intestinal health, alterations in gut microbiome, impact on immunology and finally carbohydrate metabolism and homeostasis.	**Assoc Prof Yusuf Ali** Yusuf.ali@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp00609 **Assoc Prof Zaher Judeh** **(Co-sup)**
10.2	**NIE, Exercise Physiology** **Nutritional intervention and the impact on muscle health in elderly health** This project aims to molecularly dissect pathways that are altered under (i) intermittent fasting conditions and (ii) plant-based nutritional intake. These dietary interventions are increasingly being suggested as disease-modifiers, but the molecular mechanisms that support these claims are still not well-defined. With a focus on insulin sensitivity, immunology and metabolic organ homeostasis and health, the candidate will undertake a series of in vitro and in vivo experiments to understand the role of intracellular lipid regulation response to both dietary interventions. In collaboration with exercise physiologists from the National Institute of Education, candidate will also undertake a human study to validate translation and clinical relevance.	**Assoc Prof Yusuf Ali** Yusuf.ali@ntu.edu.sg **Website** https://dr.ntu.edu.sg/cris/rp/rp00609 **Assoc Prof Steven Burns** **(Co-sup)**