Genome Institute of Singapore (GIS)								
No.	**Department**	**A*STAR Supervisor's Name**	**Designation**	**Email**	**Project Title**	**Project Description**	**Degree Awarded By Upon Graduation**	**Website Link (if any)**
1	Laboratory of Translational Cancer Biology	Dr Tam Wai Leong	Group Leader, GIS, A*STAR; Principal Investigator, Cancer Science Institute of Singapore, NUS; Adj Asst Prof at Dept of Biochemistry, Yong Loo Lin School of Medicine, NUS; Adj Asst Prof at School of Biological Sciences, NTU;	tamwl@gis.a-star.edu.sg	Development of genome-wide CRISPR genetic screens for the identification of immune gene functions in cancer	CRISPR gene editing is a powerful genetic tool for the functional studies of putative disease-contributing and disease-causing genes. This breakthrough approach, which was awarded the Nobel Prize in 2020, may be applied on a whole-genome scale for systemically ablating every gene in the genome, individually, for the discovery of novel gene functions in various disease settings, including cancer. In the past five years, understanding the role of immune cells in driving cancer evolution and learning to harness the power of our immune system to fight cancer is of immense research and medical interests. T-lymphocytes (T-cells) and macrophages are major immune cell types of clinical and translational interests. In this project, we propose to develop a whole-genome CRISPR gene editing platform for the study of immune gene functions. The discoveries will inform on the precise modulation of specific genes in T-cells or macrophages, in animal models, for resurrecting immune responses to fight cancer.	NUS/NTU/SUTD	https://www.tamlab.org
2	Laboratory of Precision Cancer Medicine	Dr Yu Qiang	Senior Group Leader, GIS, A*STAR; Adjunct Professor at NUS;Adjunct Professor at Duke-NUS School of Medicine, NUS	yuq@gis.a-star.edu.sg	Modulation of tumor immun microenvironment to improve efficacy of cancer immunotherap	This project aims to understand the molecualr mechanims of immun escape in metastatic breast cancer and develop novel therapetuic modalities that can boost hypoxic tumor immune microennvironment to increase response to immunotherpay.	NUS/NTU/SUTD	
3	Laboratory of Precision Cancer Medicine	Dr Yu Qiang	Senior Group Leader, GIS, A*STAR; Adjunct Professor at NUS;Adjunct Professor at Duke-NUS School of Medicine, NUS	yuq@gis.a-star.edu.sg	Epigentic solution to overcome anti-HER2 immunothearapy and biomarker development	Epigenetic mechanisms leading to deficiency of anti-tumor response in HER2+ tumors will be investigated and the novel treatment strategy including novel epigentic drugs will be developed to overcome anti-HER2 immunotherapy	NUS/NTU/SUTD	
4	Laboratory of Imagenomics	Dr Chen Kok Hao	Senior Research Scientist, GIS, A*STAR	chenkh@gis.a-star.edu.sg	Single cell transcriptome imaging	This is an interdisciplinary project that involves biochemistry, optics, engineering, and biology. We are developing spatial-omics methods--multiplexed error robust fluorescence in situ hybridization (MERFISH)--to study gene expression in cells in their native tissue environment. MERFISH allows us to locate and quantify up to 1,000s of RNA species in every single cell. To profile RNA in tissues, we used a split-probe design to achieve enhanced specificity. Split-FISH reduces off-target background fluorescence, decreases false positives, and enables accurate profiling in uncleared tissues. Read more at https://khchenlab.github.io/	NUS/NTU/SUTD	https://khchenlab.github.io/

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5	Laboratory of Computational Transcriptomics	Dr Jonathan Goeke	Group Leader, GIS, A*STAR	gokej@gis.a-tar.edu.sg	Algorithms for fast segmentation of Nanopore sequencing data		NUS/NTU/SUTD	www.jglab.org; https://github.com/GoekeLab
6	Laboratory of Computational Transcriptomics	Dr Jonathan Goeke	Group Leader, GIS, A*STAR	gokej@gis.a-tar.edu.sg	Development of a machine learning model to study RNA modifications using Nanopore sequencing		NUS/NTU/SUTD	www.jglab.org; https://github.com/GoekeLab
7	Laboratory of Computational Transcriptomics	Dr Jonathan Goeke	Group Leader, GIS, A*STAR	gokej@gis.a-tar.edu.sg	Algorithms f for ultra-fast processing of Transcriptomics data		NUS/NTU/SUTD	www.jglab.org; https://github.com/GoekeLab
8	Laboratory of Molecular Epigenomics & Chromatin Organization	Dr Roger Foo	Senior Group Leader, GIS, A*STAR; Professor at YLLSoM, NUS and NUH	foosyr@gis.a-star.edu.sg	High throughput screening for transcriptional regulators of metabolic shift during cardiac disease	Under normal circumstances, the adult heart derives most of its energy from β oxidation of fatty acids, however, during conditions of cardiac stress and heart failure, there is a shift in cardiac energy substrate utilization from fatty acids to glucose. This alteration in metabolism plays a key role in the progression of heart failure, hence understanding the transcriptional regulators of this metabolic shift may help identify pathways that are activated in cardiac stress and thereby help uncover novel therapeutic targets. This project uses genomics, and epigenomics to discover transcriptional factors important for the change in metabolism as well as their target genes.	NUS/NTU/SUTD	

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9	Laboratory of Molecular Epigenomics & Chromatin Organization	Dr Roger Foo	Senior Group Leader, GIS, A*STAR; Professor at YLLSoM, NUS and NUH	foosyr@gis.a-star.edu.sg	CRISPR-mediated gene based therapy for cardiac disease	Majority of the cardiac disease-associated genetic variants uncovered through GWAS studies are found in regulatory regions, and these genetic variants often regulate disease progression by modifying expression of their target genes. As these regulatory regions are often tissue and context-specific, they represent potential targets for personalized and precision medicine. Our lab has performed ChIP-seq , ATAC-seq and HiChIP to identify unique enhancers for key cardiac genes implicated in heart failure. This project aims to use CRISPR-mediated activation and inhibition of enhancers to regulate expression of important genes and thereby rescue heart failure phenotype in mouse models	NUS/NTU/SUTD	
10	Laboratory of Molecular Epigenomics & Chromatin Organization	Dr Roger Foo	Senior Group Leader, GIS, A*STAR; Professor at YLLSoM, NUS and NUH	foosyr@gis.a-star.edu.sg	Enhanced Single Cell Transcriptomics for New Biomarkers and Targets in Cardiovascular Ageing	Cardiovascular disease (CVD) is the primary cause of morbidity and mortality globally. Age is a fundamental predictor of CVD risk, and as populations age, associated social and economic burden is projected to become increasingly severe. Survivors of acute myocardial infarction (MI) may develop progressive deterioration of cardiac function and heart failure (HF), prognosis for which remains worse than most cancers. New platforms for biomarker and drug discovery are urgently needed.We propose to leverage an advanced sequencing protocol, developed in our lab, to identify novel age-associated and disease-relevant cardiac cell types, states, interactions, biomarkers and drug targets. This will begin with a comparison of MI disease response in young and aged mice, at single cell resolution, with key findings later validated in banked human patient tissue samples.	NUS/NTU/SUTD	

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11	Laboratory of Metagenomic Technologies and Microbial Systems	Dr Niranjan Nagarajan	Associate Director and Senior Group Leader, GIS, A*STAR; Associate Prof at SOC, NUS; Associate Prof at the Yong Loo Lin School of Medicine	nagarajann@gis.a-star.edu.sg	Systems modelling of microbial communities, Microbial interactions in the skin microbiome	Human skin is resided by diverse bacterial and fungal species, which form ecosystems by interacting with each other and the host. Despite the efforts spent in generating sequencing data to characterize the skin microbiome across different sites of the human body, the function of various species and how a disrupted microbiome is linked to skin diseases (e.g. eczema) remain to be understand. Our lab has recently developed algorithms (BEEM and BEEM-Static) for inferring systems biology models from microbiome data, and we are applying the methods to learn how skin microbes interact with each other and how the models inferred could be used to stratify hosts into groups with distinct skin microbial ecologies. We have recently collected skin microbiome samples from a large cohort of Asian subjects (>3000), which is ideal for constructing generalizable models to describe the ecology and predict the dynamics of Asian skin microbiomes. In this project, we intend to extend our algorithms to integrate multiple types of data (e.g. metabolomic and phenotypic data) in order to elucidate more insights into the mechanisms of host-microbe interactions and roles of microbiome in skin diseases.	NUS/NTU/SUTD	
12	Laboratory of Metagenomic Technologies and Microbial Systems	Dr Niranjan Nagarajan	Associate Director and Senior Group Leader, GIS, A*STAR; Associate Prof at SOC, NUS; Associate Prof at the Yong Loo Lin School of Medicine	nagarajann@gis.a-star.edu.sg	Machine learning for uncovering biomarkers of treatment and response in cancer	Cancer is a genetic disease arising from the accumulation of mutations in cells, culminating into unchecked cell growth. A computational model is needed for analysing complex patient molecular information and uncovering biomarkers that can be utilised for predicting effective treatments to inhibit cancer metastasis and drug resistance. Several studies have been focusing on utilising publicly available molecular and drug response data from standard cancer cell lines. Diverse types of machine learning models, ranging from traditional linear regression to deep learning, have been proposed for predicting drug response. Although many of these models showed promising accuracy, they were typically trained and validated only on cell lines from in-vitro studies, limiting translation applicability to clinical applications. Furthermore, the standard cancer cell lines do not harbour the intra-tumour heterogeneity associated with clinical samples. To overcome these challenges, we aim to integrate public cancer cell line data generated from different experimental setups into a comprehensive drug response resource. This will allow us to uncover biomarkers of treatment across experimental setups including those for patient-derived cancer cell line models (PDCs). Single-cell technologies would be utilised to capture intra-tumour heterogeneity present in PDCs and consolidated into the database. The comprehensive drug response resource, molecular information of PDCs, and single-cell data generated in this project would be critical to the development of a machine learning model to predict drug response in precision oncology.	NUS/NTU/SUTD	

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13	Laboratory of Metagenomic Technologies and Microbial Systems	Dr Niranjan Nagarajan	Associate Director and Senior Group Leader, GIS, A*STAR; Associate Prof at SOC, NUS; Associate Prof at the Yong Loo Lin School of Medicine	nagarajann@gis.a-star.edu.sg	Nanopore sequencing based analysis of complex microbiomes	Whole metagenomic sequencing is a popular means of profiling the complex microbial landscape in different environments. Metagenomic data can be leveraged to assemble numerous microbial genomes. This is important for many applications such as microbial strain tracking, novel species identification, antibiotic resistance gene analysis and biosynthetic gene cluster mining. As such, there is considerable value in developing and using more accurate metagenomic assembly methods to answer biological questions. Illumina and Nanopore sequencing are two commonly used ways of sequencing the microbiome, each with their pros and cons for metagenomic assembly. The former produces relatively large quantities of short reads which provide good coverage of numerous microbes at high accuracy, but produces less contiguous genomes. The latter is advantageous for genome assembly due to increased read length, but suffers from reduced coverage and increased base calling errors. To overcome these limitations, our lab has recently published a hybrid assembler (OPERA-MS), which combines the advantages of using short and long read data. We have since used OPERA-MS to assemble even higher quality “platinum” metagenomes. One important dataset from our lab, is the collection of > 4400 high quality metagenomes assembled from > 100 healthy Singaporean gut microbiomes. We are in the process of cataloguing novel species and strains from these metagenomes, as well as mining them for biosynthetic gene clusters which are “unique” to our South-East Asian population. The OPERA-MS tool and accompanying utilities can be readily extended to high-resolution profiling of microbiomes from other body sites and environments. This, coupled with our expertise in microbiome modelling and statistical analysis, enables us to answer various questions about the functional role of the microbes around us, and ultimately provide the basis for rational modulation of the human microbiome.	NUS/NTU/SUTD	

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14	Laboratory of Metagenomic Technologies and Microbial Systems	Dr Niranjan Nagarajan	Associate Director and Senior Group Leader, GIS, A*STAR; Associate Prof at SOC, NUS; Associate Prof at the Yong Loo Lin School of Medicine	nagarajann@gis.a-star.edu.sg	Evolution of antimicrobial resistance in the gut microbiome	The human gut is inhabited by trillions of bacteria that carry out several vital functions, such as the production of essential vitamins, degradation of oligosaccharide and regulation of homeostasis. Alterations in the composition of gut microbiota are often associated with the development of metabolic and neurological diseases. Antibiotics usage exerts profound effects on the gut microbiota and its prolonged use provides a selection pressure for microbe populations to evolve and develop resistance. Evolved genes that confer such antibiotic resistance can be disseminated widely amongst the residents of the gut through processes such as horizontal gene transfer. Antimicrobial resistance (AMR) has emerged into a common global concern. It is, therefore, essential to understand the mechanisms of AMR and how the gut ecology is perturbed by antibiotic usage. We have recently published a metagenome-wide association study, where we analysed hundreds of metagenome profiles and identified key species driving the gut recovery process post antibiotic treatment. We aim to extend this project to understand how taxonomic composition and diversity would shape the evolutionary trajectory of AMR and extent of spread of AMR genes in the gut microbiome. These insights would be critical for the development of pre- and probiotics that can mitigate the impact of antibiotics use.	NUS/NTU/SUTD	

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15	Laboratory of Bacterial Genomics	Dr Swaine Chen	Group Leader, GIS, A*STAR; Associate Professor at YLL SoM, NUS	slchen@gis.a-star.edu.sg	Explaining the 2015 GBS yu sheng outbreak in Singapore - and ongoing GBS infections	The largest reported outbreak of group B Streptococcus (GBS) infections occurred in Singapore in 2015, involving over 300 cases of bloodstream infections. This outbreak was associated with consumption of 魚生 (yu sheng), a dish made from sliced raw fish and served with rice porridge by food stalls. GBS is found in approximately 30% of healthy adults and is a common pathogen among vulnerable populations, such as neonates and the elderly. GBS is known to colonize the human gastrointestinal tract and colonization has been linked to fish consumption. However, foodborne transmission leading to invasive disease had not been reported prior to this outbreak. One clone of GBS, referred to as ST283, was responsible for this outbreak. The existing global molecular surveillance of GBS indicates that ST283 GBS is almost exclusively found in Southeast Asia in both humans and fish. This project uses genomics, genetics, microbiology, and an animal model of infection to discover why ST283 GBS is so proficient at causing disease in humans and why it is well adapted to aquaculture.	NUS/NTU/SUTD	https://twitter.com/swaine_chen/status/1038085886766866433
16	Laboratory of Bacterial Genomics	Dr Swaine Chen	Group Leader, GIS, A*STAR; Associate Professor at YLL SoM, NUS	slchen@gis.a-star.edu.sg	Applying single cell genomics to gain new insights into recurrent urinary tract infection, potentially leading to novel treatment strategies	Urinary tract infections (UTIs) are among the most common infections of humans and a major reason why people take antibiotics. This, in turn, leads to higher antibiotic resistance rates. One open problem in the UTI field has been trying to understand intracellular bacteria during infection. The primary clinical problem in treating UTI is that for some patients, UTIs recur frequently, despite sometimes prolonged courses of antibiotic therapy. From studies in a mouse model of UTI, we know that UPEC are able to bind to and invade the bladder epithelial cells during a UTI. While the majority of bacteria during an acute infection are extracellular and present in the urine in the lumen of the bladder (which makes them easy to isolate, monitor, and treat), the subset of intracellular bacteria within the bladder epithelial cells is relatively resistant to antibiotic treatment and host immune defenses. These intracellular bacteria can therefore persist for weeks to months in the bladder (presumably causing no symptoms); upon reactivation, they can cause recurrent UTI. Intracellular bacteria have been visualized in mouse bladders and in mouse and human urine samples (from epithelial cells that have sloughed off into the urine). However, the low numbers of intracellular bacteria (compared with extracellular bacteria during acute UTI), their embedding within the host tissue, and numerical population bottlenecks during their formation has rendered standard genome-wide approaches incapable of providing molecular information on these intracellular bacteria. To address this knowledge gap, we are applying advances in single cell genomics to understand how UPEC are able to enter and survive in the intracellular niche. Some of our genetic and protein engineering tools are crucial for this work, enabling us to manipulate and visualize clinical strains of UPEC.	NUS/NTU/SUTD	https://swainechen.github.io

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17	Laboratory of Bacterial Genomics	Dr Swaine Chen	Group Leader, GIS, A*STAR; Associate Professor at YLL SoM, NUS	slchen@gis.a-star.edu.sg	Using genomics to characterize and solve new outbreaks of infectious disease	We performed the genomics analysis of the S. agalactiae strains from a 2015 outbreak in Singapore, demonstrating a definitive microbiological link between strains causing invasive disease (bacteremia and meningitis) in human patients and strains present on epidemiologically linked raw fish samples (Figure 1 below). This outbreak was the first definitive demonstration that S. agalactiae could be transmitted through consumption of contaminated food. A second major project was a collaboration with a veterinary group studying Campylobacter-mediated abortion in livestock in the US. We helped with genomics analysis of two data sets: a broad sampling of animal isolates and a set of strains derived from an experimental sexual genetics experiment performed in guinea pigs. Our analysis of the first data set helped verify the clonality of the C. jejuni strain causing abortion over a period of 15 years in the US; our analysis of the second data set led to the identification of a single gene that was both necessary and sufficient for C. jejuni to cause abortion in a pregnant guinea pig infection model. The finding that one gene was responsible for enabling C. jejuni to cause abortion provided a unique opportunity: we could screen genomics techniques, looking for any analyses that, based only on C. jejuni genome sequences, could discover the true abortion-causing gene. We found one analysis, a population genetics statistic referred to as Fu's Fs, that predicted porA as having the highest signal genome-wide for driving population expansion. Furthermore, we learned that elimination of recombination was crucial, and that sequences only from disease-causing isolates (and no background, non-disease causing isolates) were required. The signal in Fu's Fs, according to theory, indicates that porA is conferring a fitness advantage, or is under positive selection, which is driving the population expansion. We now for the first time have a fully computational technique that might provide direct, specific information about why certain bacteria are able to cause disease or how they evolved to be pathogenic. A key advantage of using Fu's Fs is that we only need disease-causing isolates, or those isolates that are sampled from a rapidly expanding (presumably successfully virulent) population. This is precisely the bias that exists in current sequencing projects, enabling us to envision broad testing of this technique on public data sets for a variety of pathogenic bacteria.	NUS/NTU/SUTD	https://swainechen.github.io
18	Laboratory of Bacterial Genomics	Dr Swaine Chen	Group Leader, GIS, A*STAR; Associate Professor at YLL SoM, NUS	slchen@gis.a-star.edu.sg	Developing sexual genetics in E. coli as a new, complimentary engine for synthetic biology applications	Genetics has been a cornerstone of biological discovery, leading to understanding, diagnosis, and treatments for numerous human diseases. The history of genetics traces its roots to Gregor Mendel's iconic experiments hybridizing pea plants; a direct line to powerful genetic systems in Drosophila and mice has enabled breakthroughs ranging from congenital disease to cancer. Building on the power of genetics in model systems, genetics in human populations leverages the same theory and basic techniques (association of DNA sequence variation with phenotypes) to understand complex phenotypes and conditions, most recently with the advent of large scale genome-wide association studies (GWAS). The technical performance of genetics has long been enabled by advances in technology; for example, GWAS was accelerated first by genotyping chips and now high throughput DNA sequencing. The Chen lab has developed several genetic techniques, in particular focusing on general tools that can be used in wild-type strains of E. coli in addition to the "easier" lab-adapted strains traditionally used for synthetic biology. These tools now, for the first time, enable access to the power of sexual genetics combined with high throughput genomics in Escherichia coli, the most well studied bacterium and most important chassis organism for synthetic biology. The marriage of sexual genetics with E. coli enables unprecedented opportunities for research discovery (which requires a robust resource supply chain) and for developing and marketing boutique, purpose-built custom chassis for the broader biotechnology industry.	NUS/NTU/SUTD	https://swainechen.github.io

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19	Laboratory of Synthetic Biology and Genome Editing Therapeutics	Dr Chew Wei Leong	Senior Research Scientist, GIS, A*STAR	chewwl@gis.a-star.edu.sg	Developing new genome & epigenome editing technologies and therapeutics	1. To develop genome and epigenome editing systems via biomining and molecular engineering, so as to conduct new forms of edits. 2. To utilise the developed technology to correct a disease indication in the appropriate organoid or animal model. 3. To evaluate the performance specifications so that the technology could be used in cell engineering settings beyond therapeutics.	NUS/NTU/SUTD	http://chewlab.github.io
20	Laboratory of Single-Cell Spatial Neuromics	Dr Liu Jinyue	GIS Fellow, A*STAR	liu_jinyue@gis.a-star.edu.sg	Analysis of gene expression patterns and organization in brain disease models	Brain organization underlies many aspects of sensory functions, physiology and mental health. For instance, brain mis-wiring is a precursor to many atypical mental states like neurodevelopmental disorders. This project will explore new ways to study brain organization and map out changes across healthy and diseased mental states.	NUS/NTU/SUTD	

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21	Laboratory of AI in Genomics	Dr Mile Sikic	Group Leader, GIS, A*STAR	mile_sikic@gis.a-star.edu.sg	Self-taught AI for genome assembly	One of the main challenges in genomics is genome assembly - the determination of genome sequence using sequenced DNA fragments called reads. The standard procedure starts with sequenced DNA fragments called reads. We mutually overlapped them to construct an assembly graph. A path through this graph has to be found—this path represents a final sequence that corresponds to an individual's genome. However, there are no algorithms that would accomplish this in a reasonable amount of time, and it is necessary to use heuristic approaches. We propose using the latest advancements in deep learning to locate critical patterns in the assembly graphs and reduce the need for heuristics. A candidate would develop models based on graph neural networks that have proved to learn in the space of algorithms. At later stages, we would also use reinforcement learning methods similar to the ones used in Alpha Zero. We expect this approach will lead to more accurate assembly genomes. Our group is one of the leading groups in the world in genome assembly. In our work, we collaborate with researchers from companies such as DeepMind, Intel, and NVIDIA. The project is suitable for candidates with a degree in computer science, statistics, or mathematics.	NUS/NTU/SUTD	https://www.a-star.edu.sg/gis/our-people/faculty-staff
22	Laboratory of AI in Genomics	Dr Mile Sikic	Group Leader, GIS, A*STAR	mile_sikic@gis.a-star.edu.sg	AI for the detection of epigenetic changes	Modification of DNA nucleotides is a critical way to control the genome's function by regulating gene expression. DNA modifications contribute to diseases such as cancer, where it is used as a biomarker. It has been found to be highly predictive of age, demonstrating the value of epigenomics data to understand each patient's profile. Our group is one of the leading groups in the world in genome analysis using sequenced data. In our work, we collaborate with researchers from companies such as DeepMind, Intel, and NVIDIA. This project aims to develop deep learning models to detect the modification from raw sequencing data. Raw sequencing data is a signal measured in a DNA sequencer. Initial models would be based on self-supervised contrastive learning that recently made a breakthrough in natural language processing and proved to be more successful in language tasks than recurrent neural networks. The project will be done in collaboration with geneticists and clinicians, and it is suitable for candidates with a degree in computer science, statistics, or mathematics.	NUS/NTU/SUTD	https://www.a-star.edu.sg/gis/our-people/faculty-staff