GENOME INSTITUTE OF SINGAPORE

A Centre for Genomic Research and Innovation

INTEGRATED SCIENCES WORKING TOWARDS EXTRAORDINARY IMPROVEMENTS IN HUMAN HEALTH AND PUBLIC PROSPERITY

VISION

The Genome Institute of Singapore (GIS) is a national initiative with a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity.

As a centre for genomic discovery, GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

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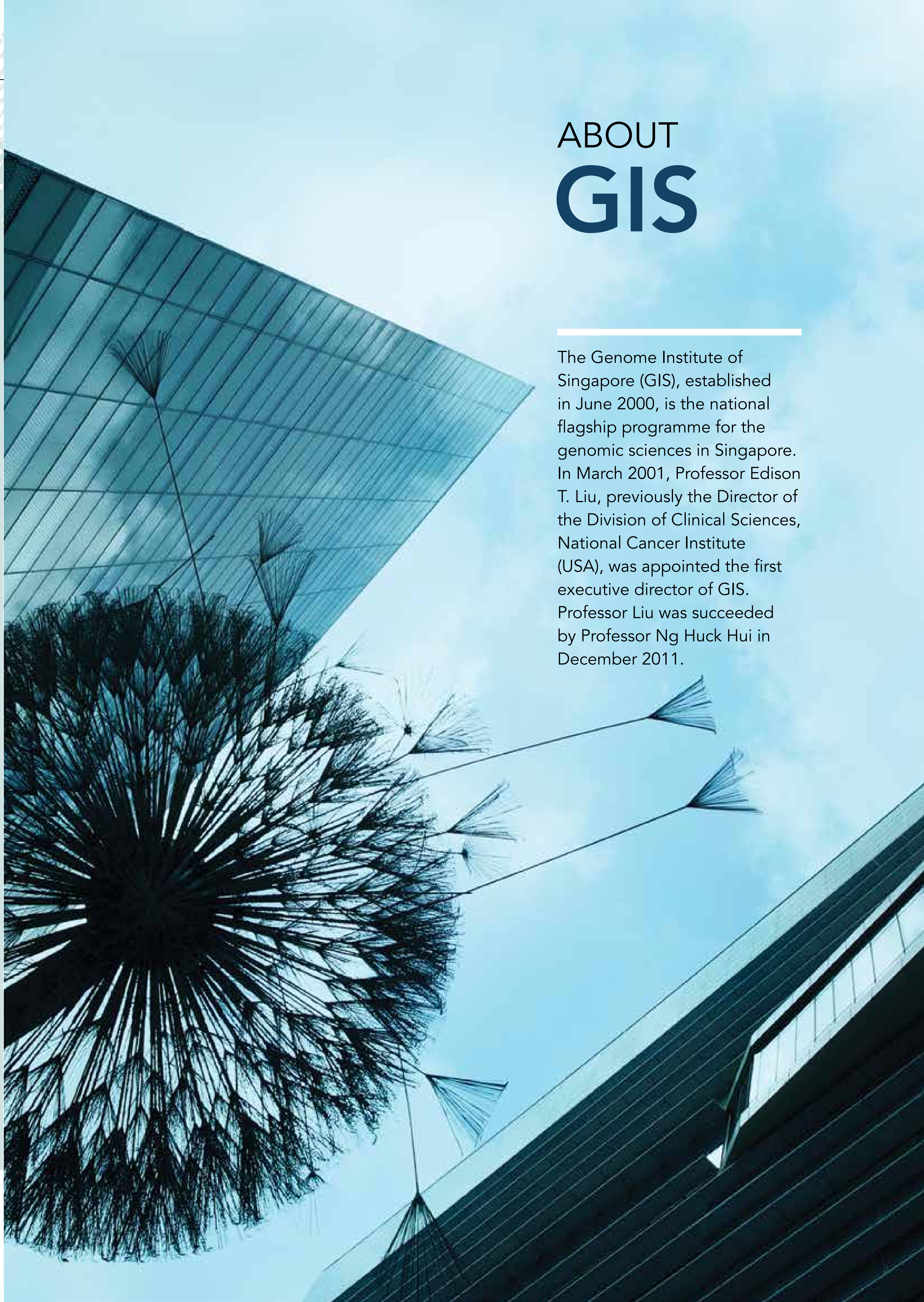
WELCOME MESSAGE FROM THE EXECUTIVE DIRECTOR

Professor Patrick Tan
Executive Director
Genome Institute of Singapore

"When the Genome Institute of Singapore (GIS) was established in 2000, the science of genomics was still in its infancy. Since then, genomics has proved its relevance to all aspects of biology and medicine. It is now possible to sequence entire populations and communities, resolve organs at the single-cell level, and develop treatments guided by genomic data. We are now able to edit genomes at will, synthesise chromosomes, and perform complex experiments in silico by harnessing the ever-growing reservoir of public-access data.

Importantly, while much has been done, much remains to be discovered as our knowledge of genomes, both human and non-human, remains incomplete. Through it all, GIS has maintained its leadership and relevance in genomic science by focusing on its three core strengths – asking the right biological questions, applying and developing cutting-edge technology platforms, and embracing multi-disciplinary team science. These core strengths have served us well, and will continue to do so in the future, as we work with our partners in the local and international ecosystem, including fellow Research Institutes, hospitals, universities, public agencies, and industry partners.

Our ultimate vision is for genomics to improve the lives of every Singaporean, in one way or another. I am excited to lead GIS in charting new frontiers in genomic science, and I invite you to join us on this exciting journey."



ABOUT GIS

The Genome Institute of Singapore (GIS), established in June 2000, is the national flagship programme for the genomic sciences in Singapore. In March 2001, Professor Edison T. Liu, previously the Director of the Division of Clinical Sciences, National Cancer Institute (USA), was appointed the first executive director of GIS. Professor Liu was succeeded by Professor Ng Huck Hui in December 2011.

BACKGROUND

GIS' second executive director, Professor Ng Huck Hui, is one of Singapore's most prominent scientists in stem cell research. He has won numerous prestigious awards including the President's Science Award (2011) for his ground-breaking work on stem cells, The Medal of Commendation (2010) for having inspired and mentored many young scientists to excel, The Chen New Investigator Award (2010) in recognition of significant contributions to his field of expertise, the National Science Award (2007) which is awarded to outstanding scientists whose research has led to the discovery of new knowledge, and the Young Scientist Award (2004) for exemplary work on gene regulation.

The Agency for Science and Technology Research (A*STAR) is the parent funding body for GIS and has a long-term commitment to create a world-class infrastructure.

In October 2003, we inaugurated our new research building, the Genome – a 7,200-sq-metre advanced facility. Set in the Biopolis, a 180-hectare biomedical city within the Buona Vista Science Hub, the Genome is adjacent to other biomedical institutes such as Singapore's Institute of Molecular and Cell Biology, the Bioinformatics Institute, the Institute of Bioengineering and Nanotechnology, the Biotechnology Institute, the Biomedical Research Council, and regional and multinational industrial R&D organisations.

The Biopolis provides an excellent environment conducive to the exchange of knowledge and collegial interactions. It was planned as a complete community that supports living, working, learning and playing: combining state-of-the-art research infrastructure with entertainment and educational facilities.

In mid 2008, the engineering research institutes were relocated to Fusionopolis, also within the one-north research and innovation hub. Together, the biomedical and engineering research arms of A*STAR form an integral part of excellence in scientific research.

GIS houses
over 300 scientists, trainees and staff.

THE MAJOR TECHNICAL PLATFORMS

of high throughput sequencing, molecular cytogenetics, bioinformatics, single cell genomics, high throughput/content screening and genome engineering have been integrated with programmes in molecular and cellular biology, computational biology and human genetics.

With these components in place, GIS is well positioned for success.

Our Approach and Our Science

Our scientific focus is to investigate questions in the realm of functional genomics and integrative biology. We exploit the intersect between genomics, cell biology, and medicine, and take advantage of the contrasting genetic history of Pan-Asian populations to uncover fundamental truths. Our biological foci on cancer biology, stem cell genomics, cellular pharmacology, and host-pathogen interactions are integrated with technology development in order to create novel solutions to difficult problems.

Consistent with our remit as a national resource, we provide the genomic infrastructure for Singapore and train new talent in this emerging field.

As the nucleating force for collaborative genomic studies in Singapore, GIS seeks to unite Singaporean scientists around collective projects of significance and extend this partnership internationally in both the academic and commercial sectors.

CULTURE

> *"Our focus on systems and integrative biology requires an organisational structure and social culture that encourages collective effort, and iterative experimentation between the wet laboratory and computational modelling."*

For these reasons, we have spent a great deal of energy in crafting the cultural state of our institute which prizes flexibility, individual intensity and collective impact. The Genome Institute of Singapore specifically recognises technology-focused scientists to be as important as biology-centric investigators, and we encourage technology experts to team with biologists to address fundamental biological questions.

Our scientific leadership structure reflects our diverse capabilities and our efforts to nurture early talent. We have principal investigators that range in expertise from basic biology to translational and medical fields. Our platform leaders handle the latest in technology and comprise some of our early career researchers (Next Generation Sequencing, Genotyping, High Throughput Phenomics, GERMS, Computational Phenomics, Single Cell Genomics, c-BIG, Genome Innovation and Genome Analytics Core).

As a national institute, GIS strives to make a difference to society by tackling various leading ageing-related health issues and infectious diseases.

We have a cohort of exceptional young scientists in our GIS Fellow programmes who are driving their own research projects that integrate into the larger GIS picture. Together, we believe the best ideas can be harnessed and pursued.

FUNDING NATIONAL CONTRIBUTIONS

In benchmarking ourselves on the international stage, we have, since our inception, competed successfully for external funds each year in the form of research grants from both local and international funding agencies such as A*STAR, National Research Foundation, National Medical Research Council, the US National Institutes of Health, and various private foundations. We have used these resources to build strong collaborative links with Singapore-based institutes of higher learning, research institutions, and medical institutions as well as US and European institutions. Within Asia, we have established strong scientific collaborations with groups in Thailand, Vietnam, and Indonesia that have also brought in significant funding to address major health issues related to emerging infectious diseases, such as dengue, tuberculosis, melioidosis, and influenza. We have also been resourceful in collaborative efforts with pharmaceutical and biotechnology companies to develop treatments and diagnostics.

Avian Influenza virus H5N1 detection kit

COMBATING INFECTIOUS DISEASES

GIS has been involved in a number of national campaigns to combat infectious diseases. As a densely populated transportation hub, Singapore is on the frontlines of any rapidly evolving global pandemic threat, as demonstrated by the Chikungunya and novel H1N1 2009 Influenza outbreaks. In addition, Southeast Asia has been the cradle of new or emerging infectious diseases, including the Highly Pathogenic Avian Influenza in 1997, Nipah virus in 1998 and SARS virus in 2003; while re-emerging threats such as dengue are also present.

With a good track record in many of these diseases, GIS expanded its infectious disease efforts and teamed up with the Ministry of Health and other government agencies, this time to tackle pandemic influenza. The GIS team sprang into action, quickly establishing a new and rapid whole genome sequencing strategy.

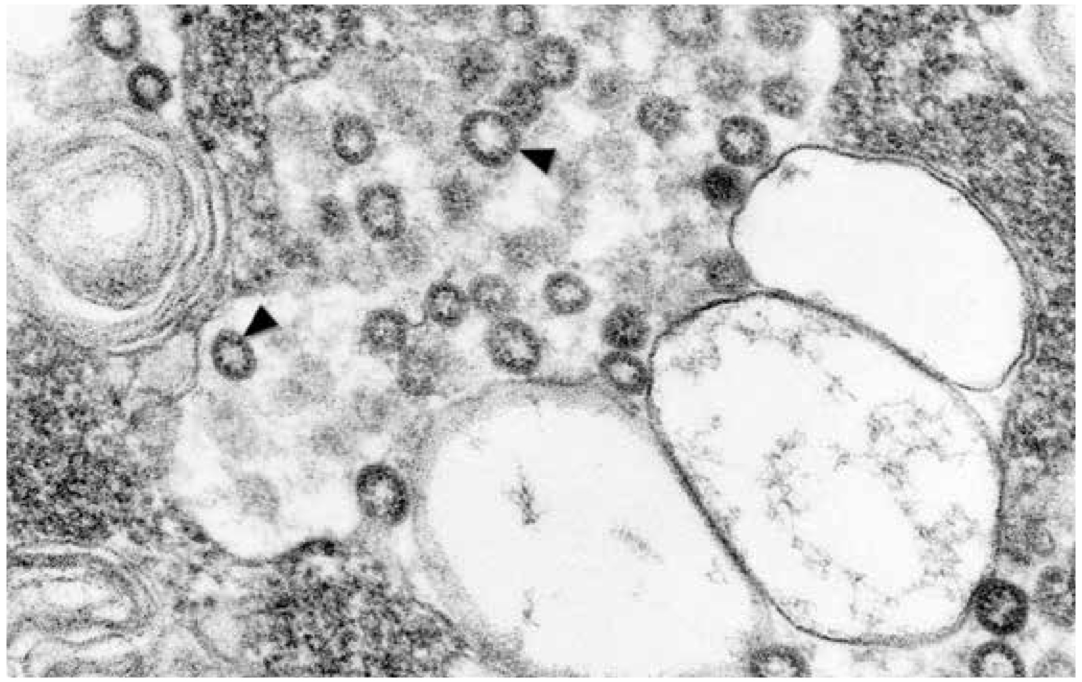
This was the basis for providing information to A*STAR's IBN (Institute of Bioengineering and Nanotechnology) about PCR detection primers and for BII (Bioinformatics Institute) to process the data to enable protein structure prediction and thus crucial information on drug resistance, virulence and potential immune or vaccine escape.

With the use of this highly sophisticated viral sequencing technology, GIS also collaborated with those at the Singapore Armed Forces (SAF), Ministry of Health, the National University of Singapore, DSO National Laboratories, and Tan Tock Seng Hospital, to ascertain a strategy to effectively contain the spread of the H1N1 (influenza A) virus; that was published in the New England Journal of Medicine. The study, conducted during the 2009 H1N1 outbreak, isolated military personnel from four camps where H1N1 infection had occurred. Of the 1,175 personnel who were determined to be at risk across these camps, 1,100 received oseltamivir (Tamiflu) prophylaxis. The result was stunning - the infection rate dropped from 6.4 percent before intervention, to 0.6 percent after intervention. The sequencing effort by GIS was able to show the direct transmission process of these viruses, and thus confirm that these outbreaks were restricted to viruses caught at the army camp, the first time that this technique has been possible.

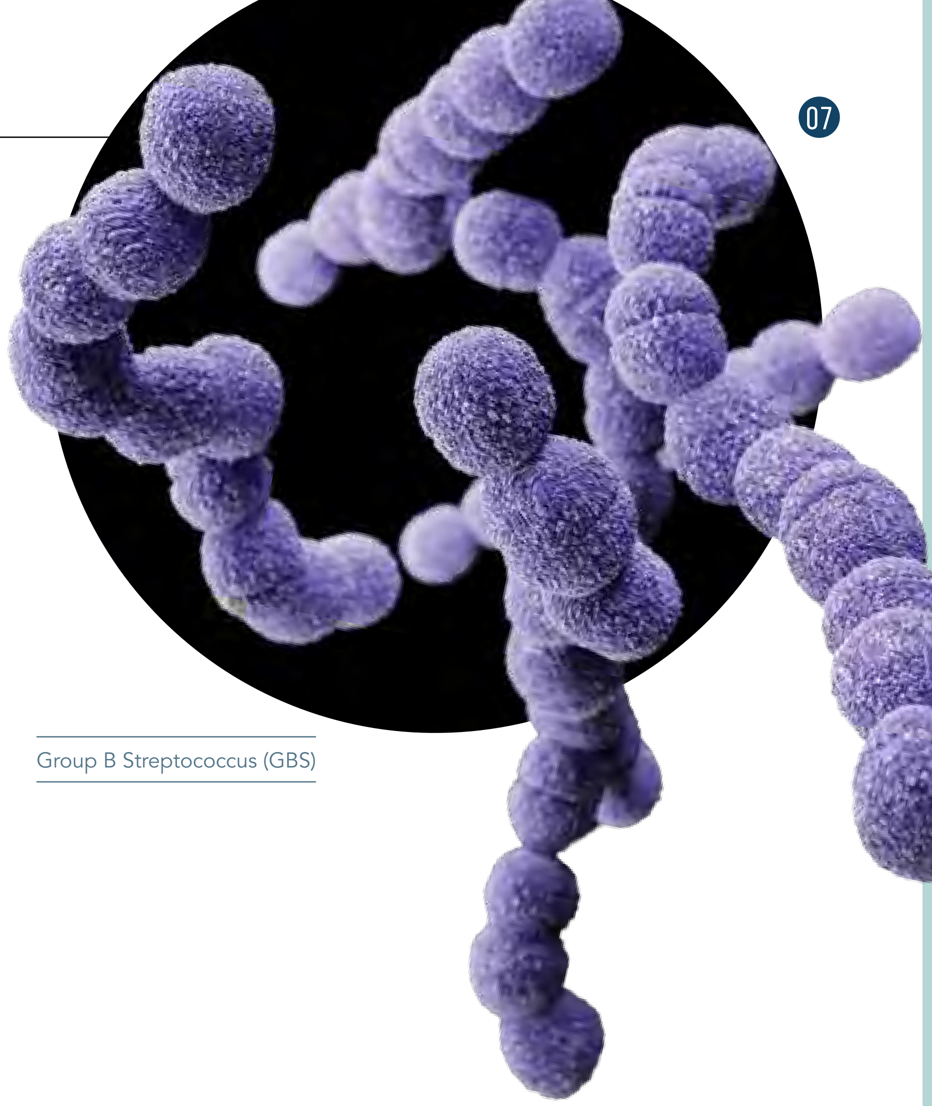
SARS CRISIS, 2003

As a national institute, we serve the nation at times of emergency. To this end, we addressed the SARS (severe acute respiratory syndrome) crisis by sequencing the SARS genome, defining viral diversity, and developing a robust diagnostic which has become the basis of the Roche SARS diagnostic kit. For these efforts, the Genome Institute of Singapore was awarded the Presidential Certificate of Commendation, and Professor Edison Liu the Commendation Medal.

At his National Day Rally in August 2003, the then Prime Minister Goh Chok Tong praised the GIS team, saying that he was proud of our researchers who worked on the genetic sequencing of the SARS virus. "In the beginning, they knew very little about the virus. They could easily have been infected… Despite the risks, more than 50 of Professor Liu's scientists raised their hands. They were from the US, Canada, France, UK, China, Taiwan, Hong Kong, Malaysia, Indonesia and Singapore—quite a collection of international talent… The scientists worked relentlessly and sequenced the SARS virus in just two and a half weeks. It was a great achievement."



Severe Acute Respiratory Syndrome (SARS)



Group B Streptococcus (GBS)

GBS OUTBREAK, 2015

In Singapore in 2015, there was a large outbreak of infections associated with eating raw fish dishes that used freshwater fish. The bacteria that caused the disease is called Group B Streptococcus, or GBS. No one had ever reported that GBS could cause infections through eating food. GIS partnered with other public agencies and local hospitals to investigate this outbreak using genomics. Together, we demonstrated that the same bacteria causing disease in humans was indeed found on the fish sold at the same hawker stalls they ate. This remarkable finding helped to prove that GBS does indeed cause severe infections due to eating contaminated food. This was a totally new mode of infection for GBS, which meant we needed to change our medical teaching about GBS as well as our education about food handling and food preparation.

ZIKA OUTBREAK, 2016

During the Zika outbreak in Singapore in 2016, the major concern was whether the mosquito-borne disease was imported from Brazil or elsewhere in the Americas, because that was where Zika was associated with birth defects after mothers became infected. To answer this question, GIS and A*STAR's Bioinformatics Institute sequenced the viral RNA for the Zika virus. In collaboration with colleagues from other local agencies and institutes, we adapted our expertise in dengue genomics to study Zika samples from Singapore. We found that the Zika outbreak here was due to a strain of Zika that was from Southeast Asia – and not from Brazil or elsewhere in the Americas. This helped to provide information to the public health agencies for communicating the risks of Zika infection, as well as to target mosquito control in Singapore.

GIS EVENT HIGHLIGHTS

C-BIG SYMPOSIUM 2019

For the second time, GIS organised a two-day c-BIG Symposium which provided a platform for discussions on Big Data and its role in precision medicine. c-BIG (the Centre for Big data and Integrative Genomics) is a multi-institute R&D consortium in Singapore comprising four of A*STAR's research institutes – GIS, Bioinformatics Institute, Institute for Inforcomm Research, and Institute for High Performance Computing. c-BIG is tasked with building the genomics data management and analytics infrastructure for Singapore's National Precision Medicine Programme (NPMP).

CELL SYMPOSIUM 2019 – SINGLE CELLS: TECHNOLOGY TO BIOLOGY

Emerging technologies for single-cell "omics" for the study of genomes, epigenomes, transcriptomes and proteomes are becoming increasingly widespread. This prompted GIS and Cell to co-organise a three-day conference, which provided a forum for sharing and disseminating cutting-edge technologies, biological insights, and biomedical applications in the field of single-cell analysis. Topics covered included atlasing cell types, perturbing and recording single cells, spatial profiling, epigenetics and multimodal profiling, data analytics, and precision medicine.

SINGAPORE NANOPORE CAMP 2018

Singapore Nanopore Camp 2018 was the seventh edition of the PoreCamp series and the first edition in Asia, having previously been held in the UK, Australia, USA and Canada, since its inauguration in 2015. It was a five-day training bootcamp based around the Oxford Nanopore Technology (ONT)'s MinION sequencing system, which had been used to monitor the Ebola outbreak in 2015, the Zika outbreak in 2016, and in July 2016, the MinION became the first sequencer in space. Hosted by GIS' Dr Niranjan Nagarajan, the workshop was a unique opportunity to get hands-on experience in generating and analysing MinION data. A field trip to the Singapore Botanic Gardens was held on the final day, when participants engaged in the sequencing and analysing of *Trametes sanguinea* (more commonly known as the lingzhi mushroom).

21ST GOLDEN HELIX PHARMACOGENOMICS DAY 2018

This international event was co-organised by SAPhIRE (Surveillance and Pharmacogenomics of Adverse Drug Reactions, a BMRC-funded programme led by Dr Liu Jian Jun), Prof Wasun Chantratita (Mahidol University, Bangkok), Assoc Prof Dr Le Thi Ly (Ho Chi Minh International University) and the Golden Helix Foundation. It featured presentations from local and international speakers on the impact of pharmacogenomics in various medical specialties, focusing in particular on the bioinformatics solutions in pharmacogenomics.

SINGAPORE-EMBL SYMPOSIUM ON PRECISION MEDICINE 2017

The Sg-EMBL symposium 2017 was held jointly by GIS' c-BIG and EMBL (European Molecular Biology Laboratory), and supported by GIS, BMRC and EMBL. The symposium consisted of a public scientific conference focused on the emerging and cross-disciplinary field of precision medicine. The programme covered a wide range of topics, spanning from computation genomics and bioinformatics to genetic and genomic databases; aiming to share the most up-to-date research trends, results, information and databases. It was a fantastic reunion for fellow scientists and offered networking opportunities for established and young investigators. There were also special meetings between members of the EMBL, including Dr Silke Schumacher (Director International Relations, EMBL) and Ms Plamena Markova (Joint Head of Government and EU Relations, EMBL) and the various Singapore representatives seeking collaborative engagements with EMBL. They were from organisations such as BMRC, GIS, NUHS, NUS, NMRC, NTU, CBIS, BII, IHPC, CSI, SBIC and IHIS.

C-BIG SYMPOSIUM 2016

An inaugural c-BIG Symposium was held to bring together thought leaders across the entire spectrum of Big Data analytics, from infrastructure to algorithms, from omics to medical records and from bench to bedside to the entire health system. The purpose of this was to spur a larger national conversation on Big Data, foster interactions across institutional borders and nucleate new initiatives. It also aimed to increase awareness of the importance of this area for precision medicine, and the challenges and opportunities that lie ahead.

INTERNATIONAL CONFERENCE ON SYSTEMS BIOLOGY 2015

GIS was one of the local partners involved in the logistics setup for the 16th International Conference on Systems Biology (ICSB 2015). The ICSB has become one of the most important forums for the global systems biology community. The annual gathering attracted top systems biologists and interdisciplinary researchers from all over the world to display and discuss the most recent achievements and discoveries.

CELL SYMPOSIUM: HUMAN GENOMICS 2015

GIS co-organised the three-day conference with Cell. It was the first Cell Symposium to be held in Singapore. The aim of this meeting was to bring together leading researchers investigating a variety of aspects related to human disease through genomic approaches, share their findings, and offer insights on future avenues for research and treatment. Some of the technological breakthroughs that were pushing this field forward were also highlighted.

FORUM ON GENOMIC MEDICINE 2015

As part of our 15th year anniversary celebration, GIS, in collaboration with local medical schools (Yong Loo Lin School of Medicine NUS, Lee Kong Chian School of Medicine NTU, Duke-NUS Graduate Medical School) organised a Scientific Forum on Genomic Medicine to discuss the impact of large-scale whole-genome sequencing analysis on biomedical research and healthcare service. Rapid development of NGS technologies, especially the ones for large-scale whole-genome sequencing, was transforming the landscape of biomedical research and potentially clinical practice. Renowned speakers from The Genomics England, UK (100K Genome Project), The Children's Hospital of Philadelphia, deCODE and Stanford University were invited to discuss how large-scale whole-genome sequencing technologies have been employed to enhance national infrastructure for healthcare service and economic development, advance the clinical management of diseases, optimise the pipeline for drug development, and pursue personalised genomic medicine. By organising an event such as this, GIS and its partners aimed to create a national platform in Singapore for discussing the impact of large-scale whole-genome sequencing analysis on biomedical research and healthcare service and exploring national strategy for advancing Genomic Medicine through adoption of such technologies.

BASESPACE WORLDWIDE DEVELOPERS CONFERENCE 2014

Illumina and GIS jointly organised the first Singapore Worldwide Application Developers meeting for BaseSpace. BaseSpace is Illumina's end-to-end genomics, cloud-based and now on-site, bioinformatics platform for next-generation sequencing. At the training workshop, participants learned how to build and launch their own bioinformatics apps on BaseSpace.

ASIAN EPIGENOMICS MEETING 2014

GIS hosted an epigenomics meeting in Singapore for the second time. Entitled “Epigenetics in Development and Diseases: 9th Asian Epigenomics Meeting 2014”, the conference was held over two days in August 2014 at the Biopolis. An equal mix of foreign and local scientific experts working in the areas of epigenetics and epigenomics spoke at this conference, which was chaired by Professor Ng Huck Hui.

2012 MERCK MILLIPORE ASIA BIOFORUM

Merck Millipore and GIS co-organised the conference themed Cancer Biology Horizons: Integrated Approaches in Understanding Systems Biologic Disease on 19 November 2012. One of the two keynote speakers at the event, Dr Lim Bing, spoke on the clinical relevance of tumour initiating cells.

CHIA-PET ANALYSIS WORKSHOP 2011: METHODS FOR A CHROMATIN INTERACTION ANALYSIS

Genomes are organised into high-order architectures for functions. However, little is known about how chromosomes are organised at molecular levels and what types of structural platforms are implemented for genome functions. The ChIA-PET method was developed to address these questions.

The five-day intensive workshop, held from 4 to 8 April 2011, covered the most critical experimental aspects in ChIP sample preparation and ChIA-PET library construction. The unique features of sequencing ChIA-PET libraries were discussed, and basic concepts for computational analysis of ChIA-PET data introduced.

PERSONALISED CANCER MEDICINE CONFERENCE 2011

A strategic collaboration between GIS and the Fritz Bender Stiftung (Germany) brought about the organising of this conference, which explored the implementation of individualised approach to medicine from basic sciences to clinical investigations. Held in Singapore from 21 to 23 February 2011, the sessions covered cancer genetics, genetics mutation, gene expression regulation, disease-specific concerns, and targeted therapeutics. Chaired by Professor Edison Liu, the conference attracted a 300-strong participation across the globe.

NATIONAL SCIENCE CHALLENGE 2010

GIS hosted the National Science Challenge 2010. This is a collaborative programme by the Science Centre Singapore and A*STAR. An annual event since 2005, it aims to revive national interest in science through a televised science quiz, and promote an interest in science among Singapore youths, targeting those under 18 years and their families. The science quiz is a series of competitions amongst Secondary 3 students from various schools, and segments include studio rounds, studio demonstration and outdoor challenge hosted by the various research institutions at A*STAR.

Filming of the final round of the 2010 competition was carried out at GIS and the Finals of the challenge was telecast in August over Channel 5. Professor Edison Liu was one of the three judges.

INTERNATIONAL KAWASAKI DISEASE GENETICS CONSORTIUM MEETING 2009

GIS hosted the inaugural meeting of the International Kawasaki Disease Genetics Consortium (IKDGC) in 2009. This was an invitation-only, closed-door meeting, held to discuss issues pertaining to, and promote, joint friendship efforts as well as the sharing of samples and data.

EPIGENETICS IN DEVELOPMENT AND DISEASES CONFERENCE: 4TH ASIAN EPIGENOMICS MEETING 2009

GIS hosted a two-day epigenomics conference, the first to be held in Singapore. It witnessed the coming together of 28 renowned speakers from Asia, Europe and the US, with a 350-strong delegation. Chaired by Dr Ng Huck Hui of GIS, the conference featured scientific sessions covering epigenomics, higher-order genome organisation, epigenetics and human disease, and challenges of epigenetic drug discovery.

The annual Asian Epigenomics Meeting is organised by The Asian Epigenome Network (comprising five members: Korea, Japan, China, Taiwan and Singapore) to foster the collaboration and exchange of scientific expertise and knowledge in the broad area of epigenomics. Each year, the country members take turns to organise an international conference.

INFECTIOUS DISEASE CONFERENCE 2008

The Infectious Disease Conference forms part of the “UK-Singapore Partners in Science” programme, which was launched in July 2005 by the UK and Singaporean prime ministers to increase scientific collaboration between our two nations in priority research areas of mutual strength. More than 200 delegates from Singapore and the region, as well as the UK, attended the conference to present and discuss developing technologies that would enable new understandings of infectious disease. The conference programme also explored the technological advances that underpin translational research, with an emphasis on genomics and applications in Southeast Asia.

AACR CENTENNIAL CONFERENCE TRANSLATIONAL CANCER MEDICINE: TECHNOLOGIES TO TREATMENT 2007

The first AACR Centennial Conference was an exciting meeting which convened more than 1,500 experts, trainees and other interested parties in Singapore to present and discuss new and developing technologies that would enable the translation of discoveries into the practice of cancer medicine. Organised by GIS and the American Association for Cancer Research, this important international conference also provided an opportunity for scientists, clinicians, policy makers, analysts, and others to increase their understanding of the future advances in biotechnology and medicine. A wide range of topics was covered during the week-long conference, including the “Advances in Cancer Therapeutics” and “New Strategies in Drug Development”.

KEYSTONE SYMPOSIUM 2005

Some 500 top biomedical research scientists and clinicians from the US, Europe and Asia were in Singapore to attend a week-long Keystone conference on “Stem Cells, Senescence and Cancer”. Organised by Keystone Symposia, the conference in Singapore was the first scientific meeting of its kind to be held outside of North America since the founding of Keystone Symposia in 1972. The meeting in Singapore was organised by an international team of renowned scientists: Dr Edison Liu of GIS, Dr Alan Colman of ES Cell International, Singapore, Dr Curtis C.Harris of the U.S. National Institutes of Health, Dr Shin-Ichi Nishikawa of the RIKEN Center for Developmental Biology, Japan, and Dr Roger R. Reddel of the Children’s Medical Research Institute, Sydney, Australia. The goal of the Keystone meeting in Singapore was to explore how the latest advances in the understanding of stem cell biology and aging can be applied to cancer cells.

5TH HUGO PACIFIC MEETING 2004

GIS had the privilege of hosting this international conference. The meeting focused on the newest discoveries arising from genomics and population studies pertinent to human disease. The theme of the conference was “Genomic Medicine and Population Health” with prominent speakers Dr Savante Paabo of the Max Planck Institute for Evolutionary Anthropology, Dr Jennifer Blackwell of the Cambridge Institute for Medical Research and Dr Raymond White of the Ernest Gallo Clinic and Research Centre. The conference was held in Singapore for the first time and it attracted over 600 participants from 30 countries.

AWARDS

> *"For outstanding contribution in the field of Parkinson's Disease, galvanising clinical research and transforming patient care through the identification of clinical biomarkers, development of novel models and therapeutics"*

(Left) Left to Right
Assoc Prof **LIM** Kah Leong, Assoc Prof Louis **TAN**,
Prof **NG** Huck Hui, Prof **TAN** Eng King

(Below) Left to Right
Dr Nirmala **RAYAN**, Mr Oliver **WORSLEY**,
Dr Kristy **PURNAMAWATI**, Mr Albert **DASHI**, Dr Abil **SAJ**

PRESIDENT'S SCIENCE AWARD 2018

*Prof TAN Eng King, Deputy Medical Director (Academic Affairs), National Neuroscience Institute; Associate Prof LIM Kah Leong, Head, Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore; Prof NG Huck Hui, Executive Director, Genome Institute of Singapore, A*STAR; Associate Prof Louis TAN, Senior Consultant, Neurology, National Neuroscience Institute*

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Professor Tan Eng King and team were recognised for their outstanding contributions in identifying clinical biomarkers, developing novel models and therapeutics for advancing the understanding and management of Parkinson's Disease (PD) over the last five years.

L'ORÉAL RESEARCH & INNOVATION STARTUP CHALLENGE 2018

Dr Oliver WORSLEY, GIS Innovation Fellow, and Mr Albert DASHI, PhD Student, Human Genetics

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Dr Worsley and Mr Dashi, co-founders of Sequential, took first place in the competition and were awarded for best start-up pitch and innovative idea. The duo focus on genetics and an environmental approach to personalised cosmetic using core technology developed at Sequential to detect molecular differences in and on the skin.

CIFAR AZRIELI GLOBAL SCHOLARSHIP

Dr WAN Yue, Senior Research Scientist, Genomic Technologies

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Dr Wan was welcomed to the Canadian-based international research institute, CIFAR, as a CIFAR Azrieli Global Scholar in the Molecular Architecture of Life programme. The programme funds and supports researchers within five years of their first academic appointment, helping them build research networks and develop leadership skills.

SINGAPORE TATLER'S GENERATION T 2018

Dr LI Jingmei, Senior Research Scientist, Human Genetics

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Dr Li was featured in Singapore Tatler's Generation T 2018 list of Singapore's brightest and most promising innovators, creatives, leaders and social warriors. Together with a distinguished panel of influential industry veterans and past Generation T inductees, Singapore Tatler has curated a list comprising passionate individuals aged 40 and under from across industries, who have made a noteworthy impact in their field or on society in the last 18 months.

AMERICAN ASSOCIATION FOR CANCER RESEARCH TEAM SCIENCE AWARD 2018

Dr KHOR Chiea Chuen, Group Leader, Human Genetics

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Dr Khor was part of an Asian team of cancer researchers to be awarded the American Association for Cancer Research Team Science Award, an award that honours researchers for their global impact on cancer research.

YOUNG ENTREPRENEURS SCHEME 2017 (YES17)

Dr Nirmala RAYAN (Research Associate, Computational & Systems Biology), Dr Abil SAJ (Research Associate, Cancer Therapeutics and Stratified Oncology), Mr Oliver WORSLEY (PhD student, Human Genetics), and Mr Albert DASHI (PhD student, Human Genetics) from GIS, together with Dr Kristy PURNAMAWATI (IBN's Cardiovascular Pharmacology)

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Innovation is Creativity with Execution! This was the inspiration behind Circalis' winning project as they clinched 'Best Innovative Idea' award at the YES17 competition. Circalis, a team of early career researchers from A*STAR and the National University of Singapore, came up with a novel idea of utilising circular RNA technology to manage hair loss in two specific groups: chemotherapy patients and athletes.

YOUNG SCIENTIST AWARD 2017

Dr LI Jingmei, Senior Research Scientist, Human Genetics

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Dr Li was one of three outstanding young individuals who were recognised with the Young Scientist Award for their achievements in research and innovation. She was recognised for her research on breast cancer and her efforts to increase public awareness of the disease.

GREAT WOMEN OF OUR TIME AWARDS 2017 – SCIENCE AND TECHNOLOGY CATEGORY

Dr LI Jingmei, Senior Research Scientist, Human Genetics

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Ten extraordinary women were honoured with the award which recognises the achievements of inspiring women. Among them was Dr Li, who received the award under the science and technology category.

Dr **WAN** Yue
Senior Research Scientist
Genomic Technologies

Dr **LIU** Jian Jun
Senior Group Leader
Human Genetics

EMBO ASSOCIATE MEMBERSHIP (2016)

Prof NG Huck Hui, Executive Director, Genome Institute of Singapore

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Prof Ng was elected an Associate Member of the EMBO, making him the only associate member to be based in Singapore. The EMBO (European Molecular Biology Organization) is a prestigious organisation which aims to promote excellence in the life sciences, and which has a membership of over 1,700 leading researchers.

L'ORÉAL SINGAPORE FOR WOMEN IN SCIENCE NATIONAL FELLOWSHIP 2016

Dr WAN Yue, Senior Research Scientist, Genomic Technologies

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Dr Wan was one of two female scientists to have been awarded this prestigious 2016 L'Oréal Singapore for Women in Science National Fellowship. She was recognised for her work on the identification of functional ribonucleic acid (RNA) elements in transcriptomes through genome-wide detection of RNA structures.

YOUNG SCIENTIST AWARD 2015

Dr WAN Yue, GIS Fellow, Genomic Technologies

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Dr Wan was one of four promising young research scientists and engineers to receive the YSA, which recognises young researchers, aged 35 years and below, who are actively engaged in R&D in Singapore, and who have shown great potential to be world-class researchers in their fields of expertise.

THE WORLD'S MOST INFLUENTIAL SCIENTIFIC MINDS 2015, THOMSON REUTERS

Dr LIU Jian Jun, Senior Group Leader, Human Genetics

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Dr Liu was one of 20 Singapore scientists who made it to the list of some 3,000 researchers mentioned in The World's Most Influential Scientific Minds 2015 report, released by the Intellectual Property and Science arm of Thomson Reuters, a media and information firm.

EMBO YOUNG INVESTIGATOR 2015

Dr KHOR Chiea Chuen, Group Leader, Human Genetics

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In recognition of his exceptional research and scientific potential, Dr Khor was awarded the EMBO Young Investigator 2015.

BRANCO WEISS FELLOWSHIP 2014

Dr WAN Yue, GIS Fellow, Genomic Technologies

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Dr Wan was one of the first scientists to develop a high throughput approach to study RNA shapes in microorganisms. An aspect of the study is to look at how pathogenic microorganisms sense and respond to their environment for survival and pathogenesis, such as Listeria monocytogenes bacteria that utilises an RNA switch that encodes virulent proteins which harm the body.

SINGAPORE YOUTH AWARD 2014

Dr Iain TAN, GIS Clinician Scientist Fellow

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Dr Tan was among six to win the award in 2014. The SYA is conferred on young people who have excelled in their fields of pursuit and contributed significantly to society.

L'ORÉAL-UNESCO FOR WOMEN IN SCIENCE INTERNATIONAL FELLOWSHIP 2014

Dr LI Jingmei, Research Fellow, Human Genetics

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Dr Li was one of 15 winners of the 2014 L'Oréal-UNESCO for Women in Science International Fellowship awards. She was recognised for the research she does in breast cancer.

YOUNG SCIENTIST AWARD 2013

Dr KHOR Chiea Chuen, Senior Research Scientist, Human Genetics

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In recognition of his research excellence in the areas of genetics and heredity, Dr Khor was presented with this award by Mr S Iswaran, Minister, Prime Minister's Office, and Second Minister for Home Affairs and Trade & Industry.

Dr **LI** Jingmei
Senior Research Scientist
Human Genetics

THE OUTSTANDING YOUNG PERSONS SINGAPORE (TOYP) AWARD 2013

Dr KHOR Chiea Chuen, Senior Research Scientist, Human Genetics

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Dr Khor was one of the recipients of the TOYP (Singapore) Awards 2013. He received a merit award for Scientific and/or Technological Development.

THE CHEN NEW INVESTIGATOR AWARD 2013

Dr Patrick TAN, Senior Group Leader, Genomic Medicine

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Dr Tan was presented with the Chen New Investigator Award from the Human Genome Organization. The award reviewing committee identified his outstanding work in cancer genomics and the profiling of Asian cancers, with a particular focus on gastric cancer.

2012 RAY WU PRIZE

Dr KONG Say Li, Post-Doctoral Fellow

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Dr Kong was among 17 who received the award, and the first Singaporean recipient. The Ray Wu Prize is awarded each year to graduate students for excellence in life science research.

PRESIDENT'S SCIENCE AWARD 2011

Drs LIM Bing, Lawrence STANTON, NG Huck Hui and Paul ROBSON, Stem Cell and Developmental Biology

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Dr Lim, Dr Stanton, Dr Ng, and Dr Robson were conferred the award by H.E. President Tony Tan for their ground-breaking work on the regulatory pathways controlling embryonic stem cell pluripotency and cell fate decisions.

Prof Patrick **TAN**
Senior Group Leader
Genomic Medicine

SINGAPORE YOUTH AWARD 2010

Dr Jonathan LOH, Research Fellow and GIS Graduate Student, Stem Cell & Development Biology

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Dr Jonathan Loh received the Singapore Youth Award 2010 for his contributions to science and technology. Presented by the National Youth Council, the youth award is the nation's highest accolade for those aged 35 and under.

THE MEDAL OF COMMENDATION 2010

Dr NG Huck Hui, Senior Group Leader, Stem Cell & Developmental Biology

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Dr Ng was conferred the Medal of Commendation in 2010, for having inspired and mentored many young scientists.

Left to Right
Dr **LIM** Bing, Dr Lawrence **STANTON**, Dr Paul **ROBSON**, Prof **NG** Huck Hui

THE CHEN NEW INVESTIGATOR AWARD 2010

Dr NG Huck Hui, Senior Group Leader, Stem Cell & Developmental Biology

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Dr Ng was presented with the Chen New Investigator Award in 2010. This award is given out in recognition of two young scientists, one within the Asia-Pacific region and one globally, who have made significant contributions to their field of expertise during their early career years.

L'OREAL SINGAPORE FOR WOMEN IN SCIENCE NATIONAL FELLOWSHIPS 2009

Drs LE Thi Nguyet Minh, Post-Doctoral Fellow, Stem Cell & Developmental Biology, and Melissa Jane FULLWOOD, Post-Doctoral Fellow, Genome Technology & Biology

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GIS scientists Dr Le and Dr Fullwood received The National Fellowships initiated by beauty giant L'Oreal, with the support of UNESCO. These fellowships are awarded to recipients doing scientific research in their own countries and are part of a larger international award programme which is widely regarded as the Nobel Prize for women.

BUSINESS EVENT AMBASSADOR OF THE YEAR (2009)

Prof Edison LIU, Executive Director, GIS

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Professor Liu was presented the award by the Singapore Tourism Board for his efforts in making significant contributions to the biomedical research landscape and bringing in prominent scientific business events.

THE OUTSTANDING YOUNG PERSONS SINGAPORE (TOYP) AWARD 2009

Dr NG Huck Hui, Senior Group Leader, Stem Cell & Developmental Biology

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Dr Ng was one of the recipients for the TOYP Awards in 2009. The TOYP Award recognises young Singaporeans for their leadership, passion to succeed in their respective fields and contributions towards the development and betterment of society.

ELECTION AS ASSOCIATE MEMBER TO THE EUROPEAN MOLECULAR BIOLOGY ORGANIZATION 2008

Prof Edison LIU, Executive Director, GIS

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Professor Liu joined the ranks of the European Molecular Biology Organization (EMBO) as an Associate (Foreign) Member. The election is to recognise the efforts of outstanding researchers who have contributed significantly to advancing molecular life sciences.

NUS OUTSTANDING YOUNG ALUMNI AWARD 2007

Dr Bernard LEONG, Research Scientist, Information and Mathematical Sciences

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In recognition of his outstanding accomplishments in entrepreneurship and sustained service to the University community, GIS Research Scientist, Dr Leong was awarded the NUS Outstanding Young Alumni Award in 2007.

NATIONAL SCIENCE AWARD 2007

Dr NG Huck Hui, Senior Group Leader, Stem Cell & Developmental Biology

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In recognition of his scientific excellence in stem cell research, Dr Ng was presented with the National Science Award in 2007. This award was presented to outstanding scientists whose research has led to the discovery of new knowledge.

NUS CENTENNIAL GENESIS AWARD 2005

Dr Bernard LEONG, Research Scientist, Information and Mathematical Sciences

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Returning A*STAR scholar and GIS scientist Bernard Leong won the NUS Centennial Genesis Award for his entrepreneurship efforts in starting up a biotech company, SimuGen, specialising in gene profiling and computational biology.

GREAT WOMEN OF OUR TIME 2005 – "MOST INSPIRING WOMAN"

Dr Lisa NG, Research Scientist, Cell and Medical Biology

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GIS scientist Dr Ng was presented the "Most Inspiring Woman" award for her contributions as a scientist at the inaugural Great Women of Our Time Awards, organised by the Singapore Women's Weekly magazine.

YOUNG SCIENTIST AWARD 2004

Dr NG Huck Hui, Group Leader, Stem Cell & Developmental Biology

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Dr Ng was awarded the Young Scientist Award in 2004 for his work on gene regulation. The regulation of gene expression is important as inappropriate expression can lead to various forms of diseases, including cancer and developmental abnormalities.

RESEARCH PARTNERSHIPS

The research excellence achieved at the Genome Institute of Singapore is directed towards our vision to advance science and develop innovative technology to further economic growth and improve lives. This is made possible by the extensive collaborations with institutions in Singapore and across the globe. We have active research and development programmes with academia, hospitals, government institutes and industries. To achieve this, we work closely with our research partners to design efficient and effective project plans and craft agreements that fully meet the needs of all parties. In most cases, these projects are joint efforts that lead to shared intellectual property. Our partners would then have an opportunity to license any mutually developed IP for their own further use.

It is our collaborative approach that leads to scientific and commercial success. Partnering with GIS means that our partners gain from our capabilities: executive leadership, strategic alliances and knowledge management, deal flexibility, excellent research and development facilities, and access to translational biosciences.

The focus of each of our alliances is to create a sustainable win-win situation for all partners involved. We consider a variety of deal types: Service Agreements and Research Collaboration Agreements for both academic and industry partnerships, and Joint Labs and Co-operation Agreements for industry collaborations.

Service
This allows delivering results to a partner when a project is straightforward and does not include significant novel research. It might be a sequencing project, karyotyping agreement, data or genome analytics project or consultancy.

Research Collaboration
The institute will perform research and development together with our partners and the outcome will comprise new Intellectual Property (IP) and know-how that addresses our partners' questions and problem statements. Such a project will enhance the partner's technological edge and could result in a downstream Licensing Agreement.

Once a partnership is established, we have a Strategic Alliances and Knowledge Management department that is focused on cultivating a strong relationship throughout the partnership. The group cultivates lines of communication and establishes a governance structure.

ALLIANCES WITH INDUSTRY

The past decade has seen a substantial increase in the number and scale of industry collaborations with GIS and our partners. GIS has signed over 80 industry research collaboration agreements in the past seven years and is envisioning further partnerships with companies. Working with commercial partners is essential for translating excellent science to implementing new technologies through delivery of novel services and products.

One BioMed-GIS Centre for Integrated Molecular Diagnostics

Our broad range of scientific and technical expertise enables us to work with a wide variety of partners from large multinational companies to local start-ups. We also work with companies across diverse sectors such as consumer, precision engineering, biotech and pharmaceuticals.

Joint Lab

GIS engages with partners on a long-term strategic basis. In this case, the company sets up an R&D lab in the Genome building, with its company personnel working closely with GIS scientists on research projects. Dedicated GIS resources are accessible to our partners, and vice versa, to advance research, technology transfer and capability building for our partners.

> *GIS offers a world-class research environment, bringing together leading expertise in next-generation sequencing, molecular cytogenetics, bioinformatics, and single cell genomics, and we are delighted to work with them on this effort."*
>
> **Tito A. SERAFINI, PhD**
> *Atreca's President, Chief Executive Officer, and Co-Founder*

GIS-NovogeneAIT Next Generation Sequencing (NGS) Platform

Centre for Precision Oncology: PuRPOSE Programme

> *We allied with the GIS Translational Research group because they combine extensive molecular diagnostics assay development expertise with regulatory and commercialisation experience,"*
>
> **Dr PARK Mi Kyoung**
> *Founder of One BioMed and its Chief Technology Officer*

Co-operation

In the last few years, GIS pioneered a new model for industry collaboration – the Co-operation Agreement. This model enables a public-private partnership that harnesses industry resources and investment to accelerate our research. In this model, companies may locate their staff and equipment within GIS' dedicated facilities, where they can provide services required for our research efforts. Any extra capacity can then be directed to the provision of commercial services. This collaborative model benefits both parties.

> *The centre is the first major project for NovogeneAIT, and is an important milestone for our company. We look forward to providing high-quality sequencing services in Singapore and to advancing important research initiatives that can benefit humanity,"*
>
> **Dr LI Ruiqiang**
> *CEO of Novogene*

OUR SINGAPORE ACADEMIC AND CLINICAL PARTNERS INCLUDE:

- Changi General Hospital
- Duke-NUS Medical School
- Khoo Teck Puat Hospital
- KK Women's and Children's Hospital
- Nanyang Technological University
- National Cancer Centre Singapore
- National Neuroscience Institute
- National University Hospital
- National University of Singapore
- Singapore Eye Research Institute
- Singapore General Hospital
- Tan Tock Seng Hospital

OUR INTERNATIONAL ACADEMIC AND CLINICAL PARTNERS INCLUDE:

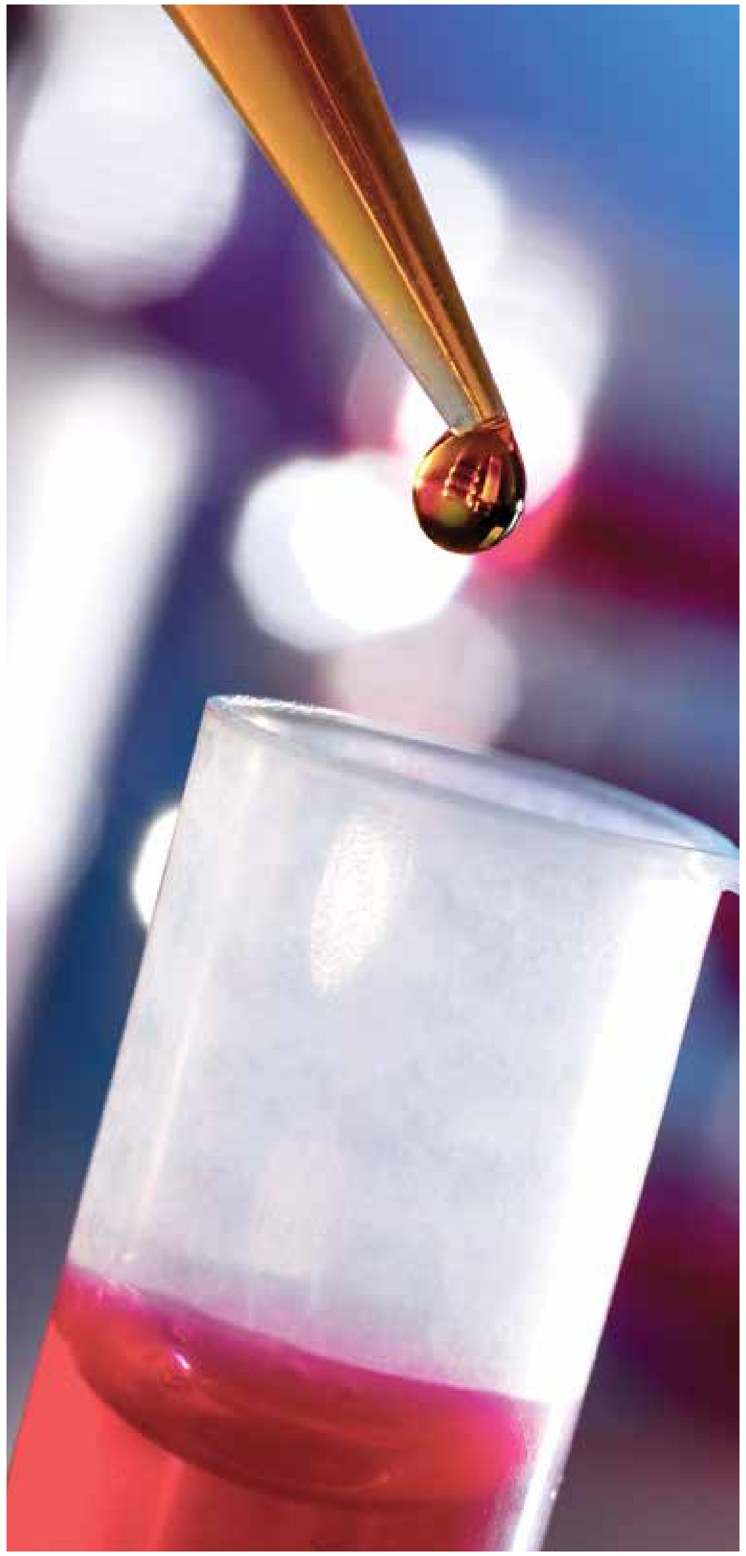
- Asan Medical Center-University of Ulsan College of Medicine (South Korea)
- Coriell Institute (USA)
- Faculty of Medicine Siriraj Hospital, Mahidol University (Thailand)
- Foundation For Industry Cooperation – University of Ulsan (South Korea)
- Hebrew University (Israel)
- Indonesia International Institute for Life Sciences – i3L (Indonesia)
- McGill University (Canada)
- National Cancer Institute (Thailand)
- Research Institute for Tropical Medicine (Philippines)
- Stanford University (USA)
- The First Affiliated Hospital, Sun Yat-Sen University (China)
- The Medical City (Philippines)
- University of Cambridge (UK)
- University of Wisconsin-Madison (USA)

Contact our Office of Strategic Alliances and Knowledge Management department at **business@gis.a-star.edu.sg** for a discussion on how GIS can support your projects.

RESEARCH THEMES

At the Genome Institute of Singapore, the different research groups work together in tandem to achieve an integrated sciences approach and focus for the purpose of working towards extraordinary improvements in human health and public prosperity.

PRECISION MEDICINE

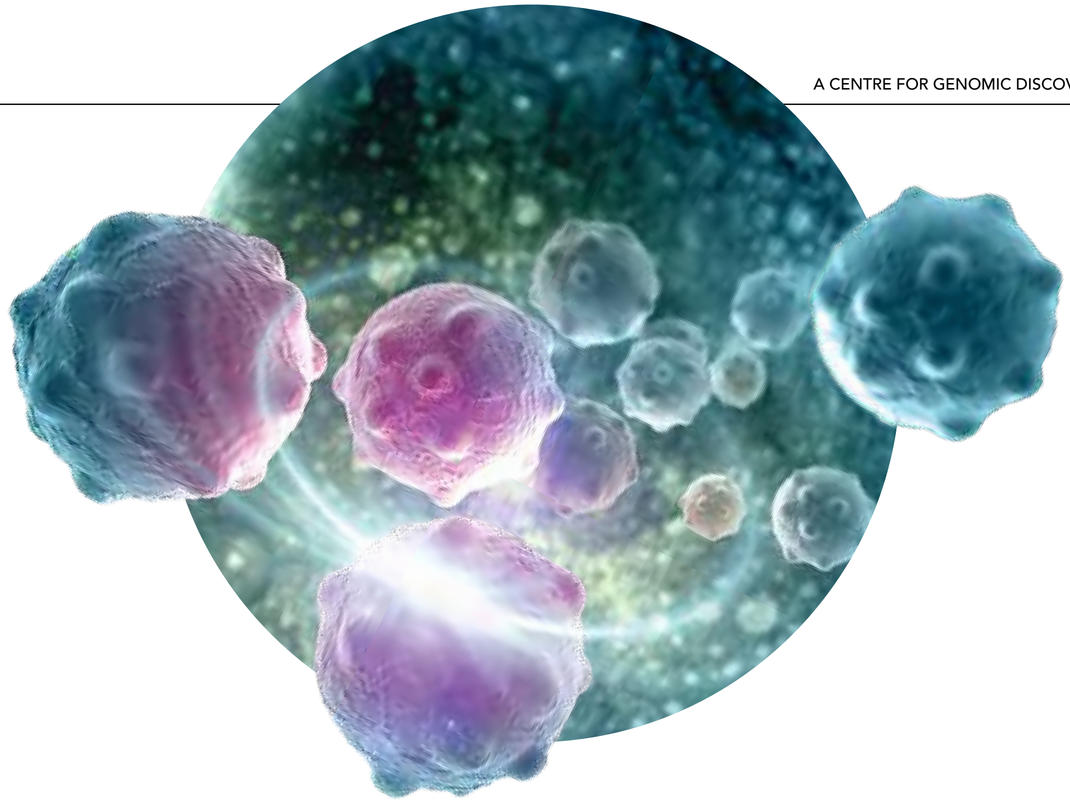


Precision medicine is an emerging approach for disease prevention and treatment that takes into account the patient's genes, lifestyle and environment. This concept is similar to blood transfusion. For example, a patient who needs blood transfusion cannot be given blood from any random donor. Instead, the donor's blood type is matched to the recipient's to reduce the risk of complications. Similarly, precision medicine allows doctors and researchers to more accurately predict which prevention and treatment strategies will work more effectively for which patient. This will not only lower healthcare costs, but also reduces the harmful side effects and consequences from unsuitable treatments.

PRECISION HEALTH

All too often, precision medicine focuses on drugs and treatments, which is essentially "sick" care. There is a need for a paradigm shift from "sick" care to "health" care. In the past decade, the Genome Institute of Singapore has been involved in many landmark genetic studies which have identified hundreds of such risk markers, for both cancer and many other diseases. These genetic risk markers collectively can create a tailored measure of an individual's risk to certain diseases. The time has come to translate knowledge into action.

In the case of cancer, while not all cancers are preventable, a third of them are. 14 million cancer cases are diagnosed worldwide every year, which means approximately 4.7 million cancer cases can be prevented from happening in the first place. And many cancers can be prevented because numerous risk factors, such as tobacco use, obesity, alcohol and diet, are modifiable. It is possible to take action. If we know exactly who are at a higher risk for certain diseases, then we will also know who will benefit more from making healthier lifestyle choices to prevent cancers from happening in the first place.



PRECISION ONCOLOGY

Cancer is a highly heterogeneous disease of the genome. Most cancer cells harbour a compendium of mutations in oncogenes and tumour suppressors that work in concert to specify the downstream molecular pathways and biological processes that lead to their genesis, and progression to treatment resistant and/or metastatic disease. Apart from the mutational signatures, there is also an increasing realisation of the importance of the cancer transcriptome (gene expression), epigenome (chromatin remodeling by histone and DNA modifications) and metabolome (cancer metabolites) in modulating the progression or evolution of cancer to refractory, metastatic disease.

Precision oncology refers to the facilitation of personalised, rational treatment choices tailored to individual patients based on their given cancer's genetic makeup, heterogeneity, and other factors such as the tumour micro-environment (TME), that can dynamically influence its gene expression signature, and hence response to different therapeutic modalities over time and space.

The eventual scope of precision oncology is to realise the prospect of evidence-driven personalised, rational therapeutics based on enhanced molecular resolution and increased mechanistic clarity.

To realise this goal, researchers at the Genome Institute of Singapore, in close collaboration with their clinical partners, have embarked on an ambitious programme to drive precision oncology that seamlessly integrates cancer genomics (accurate identification of clinically-actionable driver mutations, and gene expression/pathway signatures), with functional genomics (functional characterisation of driver events and molecular pathways) under the unified platform of next-generation advanced "screen-able" patient-derived models, including primary cells (PDC), organoids (PDO), and xenografts (PDX).

Supporting this effort is an integrated data analytics pipeline comprised of:

- Novel computational algorithms for the discovery of novel, and highly specific driver mutations and bulk/single-cell gene expression signatures predictive of drug response in the clinic;
- Neural networks-based *data analytics platform for phenotypic lead discovery* or DAPPLeD, that combines artificial intelligence (AI) with high content phenotypic screening (HCS); and
- Onco-SG, a uniform, secure, collaborative web-based data platform for precision oncology that harbours genomic and transcriptomic data from both global cancer consortia like the TCGA (more than 49K samples from 172 clinical studies) as well as local clinical studies (1895 samples, 12 studies).

Altogether, such analytical and visualisation platforms are intended to generate bigger and uniform data to enable the generation of new biological and clinical insights for the implementation of precision oncology in the clinic, and provide clinicians with a novel framework for treatment regimens that greatly benefit patients.

FUTURE TECHNOLOGY

At the Genome Institute of Singapore, our mission is to build and harness cutting-edge technologies to read and write DNA. These technologies enable us to decipher the language of life, create new biological functions, and fight diseases.

How are we building the future of DNA-reading technologies? We are already testing for biomarkers of many diseases through assaying patient-derived biopsies and bodily fluids. We can now predict, for each patient, not just the disease likelihood many months or years down the road, but also the heritability of these disease genes, and hence the likelihood of these impacting future offsprings. The sensitivities of these assays are improving with every iteration of our technologies, as we probe every molecule and every cell. As we juxtapose these precise measurements with disease types, spatial distribution within the body, and across large cohorts of human patients, we are making it possible to understand, and hence diagnose and tackle human diseases. GIS is at the forefront of developing these molecular magnifying glasses.

Illuminating the underlying mechanisms and vulnerabilities of diseases opens up enticing ways to directly fight them. We are inventing the technologies to stop these diseases. GIS has been developing CRISPR technologies to edit and correct genetic errors, thereby reversing the fundamental cause of diseases. We are making these new therapeutics better, faster, and safer. Writing DNA also makes it now possible to dissect and examine our genomes, and the genomes of many other species, in ways previously unimagined. Beyond DNA, GIS is working on ways to manipulate the multiple DNA epigenetic modifications and forms of nucleic acids that are important for proper biological function. Our technologies are the direct enablers for making cells, animals, and mini-human organs according to design. We are making it possible to engineer life.

As we explore the many unknowns in biology and medicine, we know that new technologies will empower us to better illuminate these unknowns, diagnose diseases better and faster, and treat previously untreatable diseases. Developing the future technologies for reading and writing DNA is in our DNA.

SMART NATION GENOMICS

Singapore launched its Smart Nation Initiative in November, 2014. Since then, the vision of an interconnected city – driven by networked devices and intelligent analytics that simultaneously simplify and enhance the lives of its citizens – has become popular across cities around the globe. Singapore remains a leader in the intelligent transformation of the urban environment, with its long-established advantage in national infrastructure derived from decades of intentional investment. Of particular importance are the combined advantages of size, population density, transportation infrastructure, and network connectivity throughout the island. These are a perfect base foundation for the next phase of Smart Nation upgrades with environmental sensors, mesh networks, and active and passive monitoring all tied together by advanced analytics.

Nearly coincident with the 2014 announcement of the Smart Nation Initiative, the field of genomics saw the introduction of the first handheld sequencing device – the Oxford Nanopore Technologies (ONT) MinION sequencer. In less than 10 years, genomics had achieved the physical shrinkage of genome sequencers from hulking, room-sized machines to pocket-sized portable devices, something that required 40 years for computers (from mainframes to modern mobile phones). This remarkable physical transformation finally capped an ongoing transformation (since the time that GIS was founded) of genomics into a computational and data-driven science. Therefore, while the Smart Nation Initiative was built largely on computing devices, the timing dovetailed perfectly with GIS' vision of genomics for environmental sensing driven by ever-shrinking and ever-cheaper Internet-of-Things-style (IoT) sequencing devices, embedded in the environment, and integrating with other IoT video, temperature, chemical, and environmental sensors. At GIS, we call this driving vision "ubiquitous genomics", and we see this as yet another enabling data layer to further upgrade our future Smart Nation.

GIS is laying the foundation for this urban genomics transformation in several high priority areas for Singapore: food safety, emerging infectious diseases and outbreaks, smart hospitals, and environmental monitoring. All of these feed into the larger GIS mission to improve human health, but take a broader, big data and AI perspective combined with the holistic One Health model. We have long standing partnerships with the Agri-Food & Veterinary Authority, National Environmental Agency, and Ministry of Health, covering all aspects of food safety and infectious disease monitoring and prevention. We have harnessed genomics to drive new insights into unique emerging diseases such as the Group B Streptococcus outbreak associated with raw fish in Singapore in 2015 and the 2016 Zika outbreak in Singapore. We have shown that whole-hospital monitoring, an important pilot microcosm of the ubiquitous genomics vision for all of Singapore, can provide a complete picture of microorganisms that lead to hospital-acquired infections and the spread of antibiotic resistance.

In addition, we work in close partnership with pioneering companies in this field including Oxford Nanopore Technologies. GIS hosts the full suite of nanopore sequencing technologies and combines them with novel computational and experimental techniques to leverage their unique capabilities. In 2018, we hosted the first Nanopore Camp in Asia to expand the local understanding and access to this technology, and the first Nanopore Day in Southeast Asia in conjunction with Oxford Nanopore. With these rich partnerships, combined with GIS' strengths in big data analytics and integration (represented by The Centre for Big Data and Integrative Genomics, c-BIG), we are well positioned to lead the national research effort to bring ubiquitous genomics, integrated with other Smart Nation networks, into reality.

RESEARCH GROUPS

We are in an exciting era in biology. Technological innovations are giving us the power to gather genetic and epigenetic information about cells on a genomic scale. This enables novel and alternative ways to envisage, interpret and predict cellular properties and response from molecular information.

These are the missions we place emphasis on in order to achieve excellence in science for a healthier tomorrow:

GENOMIC MEDICINE

Understanding the genetic basis of human diseases and related physiological traits is the main objective of the programme. Many of the disease phenotypes we focus on are complex diseases whose genetic risk factors are multi-factorial and work in concert with a number of environmental forces. Using both hypothesis-driven investigations and unbiased genome-wide interrogations, we are working towards identifying genomic regions or genes whose natural variations influence disease predisposition, progression and treatment outcomes.

DISEASE GENE DISCOVERY

Genetic variation plays an important role in a variety of human diseases. In human genetics, the bulk of the work lies in decoding the results from nature's experiments and annotating the DNA book of life. Genetic variants that already exist in our population are mapped to heritable diseases or traits.

One area that the Genomic Medicine programme focuses on is the identification of heritable genetic variation that underlies various common and rare diseases, particularly in the Singaporean and Asian populations. This addresses an unmet need in medical research locally and regionally, and is of crucial socio-economic importance as the population demographics shift towards an aging society.

By building up a common set of high-throughput genotyping and sequencing technologies and statistical methods through collaborative efforts, our investigation of disease inheritance and susceptibility covers diverse disease areas, including cancers (breast cancer, nasopharyngeal carcinoma, non-Hodgkin lymphoma), neuropsychiatric disorders (Parkinson's disease, schizophrenia), infectious diseases (tuberculosis, leprosy, meningococcal disease, Kawasaki disease and dengue), immunity and inflammation diseases (psoriasis, SLE, ankylosing spondylitis, IgA nephropathy, IBD), and eye diseases (age-related macular degeneration, glaucoma, pseudoexfoliation syndrome, and extreme myopia) and optic traits (central corneal thickness, optic nerve heard parameters, and intraocular pressure). We have extensive research programmes on interrogating common risk variants by genome-wide association study (GWAS) and are increasing our efforts on deciphering the contribution of low frequency and rare genetic variants to human diseases by carrying out targeted or whole exome sequencing analysis of patient cohorts, particularly the ones with either severe phenotypes or strong family inheritance. Availability and affordability of high throughput sequencing have made possible the generation of a plethora of sequencing data in a large collection of patients affected with complex and rare diseases, which will help us to achieve a good understanding on the whole spectrum of disease-related genetic variants.

Investigators

LIU Jian Jun
KHOR Chiea Chuen

With advances in artificial intelligence, the next step GIS is taking is the transformation of genetic studies from singular phenotype to multiphenotype analysis using electronic medical records.

FUNCTIONALISATION OF DISEASE RISK LOCI

We are also interested in understanding biological mechanisms that underlie these genetic risk loci by pinpointing causal variants through fine-mapping analysis and characterising their functional impacts using in vitro and in vivo model systems. By combining comprehensive association analysis and functional annotation of all the variants within the critical region of a disease risk locus, we are searching for functional variants that are the primary driver and thus the causal event of disease association. Our effort has also gone beyond regional fine mapping analysis into whole genome interrogation, for example, by analysing all the genetic variants within various transcriptional binding sites in large clinical cohorts of diseases. The importance of regulatory polymorphisms in disease development has already been clearly suggested by the fact that the disease susceptibility loci discovered by GWAS are enriched for DNA elements regulating transcriptional activities. Intersection between the new genome-wide knowledge of regulatory sequences and the rapid development of high-throughput sequencing and genotyping technologies will allow the comprehensive investigation of the role of regulatory variation in human disease development. In addition, banking on the great number of novel disease risk loci discovered by our genetic studies of common and rare diseases, we are collaborating, with other research programmes at GIS, to pursue the functional investigation of these genetic risk loci by building up in vitro cellular models of disease where genetic risk variants are introduced into disease-relevant cells derived from either embryonic stem cells (ES) or induced pluri-potent stem cells (iPS) for functional interrogation. As a complementary effort, we are also collaborating to establish in vivo model animals for the functional investigation of disease risk-associated genes or genetic variants.

TRANSLATIONAL RESEARCH AND CLINICAL IMPLEMENTATION

The knowledge gained from more than a decade's worth of human genetics studies is impacting how we approach health and medicine in a big way. Aside from twins everyone has a completely unique DNA code. Genomics provides the personalised blueprint of every individual's entire genetic make-up, which makes bespoke treatments and tailored therapy possible. The overarching goal of GIS is to translate Genomic Medicine from Science to value in precision medicine and health.

POPULATION AND EVOLUTIONARY GENOMICS AND STATISTICAL GENETICS

Since the extent and distribution of disease predisposing genetic variation in the human species today is the result of a long and complicated evolutionary, migratory, and demographic history, we are interested in investigating population and evolutionary processes affecting genetic variations in modern human populations. We have been working on assessing the extent of inter- and intra-population genomic variation and detecting signatures of positive natural selection as well as investigating genomic variation across multiple global and regional populations. In addition, we are also interested in understanding the history of introgression from archaic sister species and their distribution into extant human populations as well as the convergent evolution between domesticated species (e.g. dogs) and human beings. Such population and evolutionary genomic studies provide a unique opportunity to look at disease genetics at a much broader scale. Furthermore, we are also interested in developing novel statistical methodologies to progress beyond searching for disease association in the genome at individual SNP level, to incorporate regional or gene-based evidences and to pursue pathway analysis. To control for population stratification in disease association studies, we have also been developing methods to provide efficient and accurate ancestry estimation for both sequencing (including target sequencing, exome sequencing, and whole genome sequencing) and array-genotyping data as well as exploring novel strategies to control for population stratification and to boost statistical power for rare variant association studies by integrating information from large amounts of existing genetic data, expression data, and functional annotation data.

As Asia becomes a major therapeutic and consumer market, there is increasing demand on the genetic information of Asian populations. However, Asian populations are poorly represented in ongoing efforts of large-scale sequencing around the world.

AT GIS, WE TELL THE STORY OF SINGAPORE THROUGH GENES.

Singapore's ethnic diversity provides a good genetic representation of Southeast Asian populations. The iconic SG10K project, comprising 10,000-strong local whole-genome sequences, was built to understand genetic diversity within Singapore. As many genetic diagnoses require variant frequency information in relevant populations, SG10K will be integral in taking precision medicine from byte to bedside.

In addition, Asian genetic data is attractive to pharmaceutical and consumer genetics companies in the commercial sector, and is set to be a catalyst for industrial collaborations.

Investigators

Roger **FOO**
LI Jingmei
FOO Jia Nee

HUMAN DISEASE MODELLING

The implementation of effective treatment modalities relies on the ability to identify the appropriate and physiologically-relevant disease targets and pathways. This will greatly facilitate the translation of research discoveries into the clinical setting, as well as produce a trove of important targets for drug development and disease control.

Our research foci and infrastructure are designed to understand the genomic basis of human diseases and identify intervention points. We work in close collaboration with our clinical partners and the genome medicine group to analyse human disease samples with an emphasis on the local population. We are developing and improving genetic models of human disease ranging from stem cells and organoids to mouse models for functional genomic screens. Through functional genomics approaches, we can unravel the mechanisms behind disease initiation and progression and work towards pinpointing therapeutic targets for disease intervention and prevention in the true sense of regenerative medicine. Our models are being developed further to serve as technological platforms, enabling industry partners to do high-throughput analyses and screening.

ADVANCED ORGANOID MODELLING FOR NEURODEGENERATIVE DISEASE AND METABOLIC SYNDROME

In the region, neurodegenerative diseases and metabolic syndrome, including Parkinson's disease and fatty liver disease, are diseases with an increasing socio-economic impact in light of an ageing population and the increasing incidence of diabetes in Asia. Here at GIS, we are equipped with state-of-the-art technologies and research groups covering these disease entities.

Mini midbrain organoids developed in GIS

For example, our researchers at GIS have developed highly complex brain organoids from stem cells that can be grown in petri dishes; they closely recapitulate the disease biology which we observe in Parkinson's disease patients. Working together with the genomics and genome analytics groups, these models have enabled us to identify new disease targets as well as implement potential interventions that can help delay or reverse the disease state.

From donated patient tissues, we have also developed advanced liver organoids that faithfully mirror fatty liver disease in patients. This has enabled researchers at GIS to deeply understand how fatty liver disease arises in the Asian populations, how it can be prevented, and the type of treatment approaches clinicians can implement to control the progression of the disease.

DEVELOPING GENETIC TOOLS FOR MODELLING HUMAN DISEASES

Apart from this, we have also built sophisticated genetic tools to very precisely model the diseases that are relevant to the local and Asian populations. We have developed genetic mouse models bearing gene mutations for the various liver diseases. This has enabled us to understand how liver diseases originate and how one can intervene.

We further take advantage of recent advances in genetic editing and genome engineering technologies. Using CRISPR gene editing approaches, we are able to precisely introduce mutations into the stem cells and organoids we develop. This allows us to model disease in a petri dish. Combining these with screening platforms, we are equipped to identify new pathways implicated in the diseases, as well as discover new drugs that may be useful for patients.

Investigators

NG Huck Hui
Torsten **WUESTEFELD**
TAM Wai Leong
Swaine **CHEN**

PRECISION ONCOLOGY

Precision Oncology is about "giving the right drugs, to the right patients, and at the right time". The promise of precision oncology is to tailor clinical care of cancer patients (treatment and prevention) to each person's unique genetic makeup, their lifestyle and their environment.

Researchers at GIS aim to turn cutting-edge cancer research into innovations and effective treatment modalities. We identify novel and actionable therapeutic targets, as well as develop novel therapeutic and diagnostic modalities by integrating Cancer Genomics and Functional Genomics under the unified platform of next-generation advanced patient-derived models (primary cancer cell lines and tumour organoids). Through the implementation of these contemporary and advanced technologies, GIS researchers hope to provide clinicians with a new framework and new therapeutics in the treatment of cancer.

ADVANCING TREATMENT WITH PATIENT-DERIVED TUMOUR "AVATAR" MODELS

Precision oncology/medicine requires treatment individualisation, taking into account not only patient and tumour factors, but also intra-tumour heterogeneity and tumour evolution through time.

We believe that the next generation of precision drugs will come from the development of physiologically relevant "real-time" models of individual patient-specific tumours that mimic tumour pathology, and progression. These models serve as a powerful personalised screening platform for clinical genomics-informed predictions for genetic and therapeutic vulnerabilities that can be implemented in the clinic.

With that in mind, GIS researchers have successfully developed a suite of patient-derived tumour models (more than 150) from a vast variety of solid cancers (colorectal, liver, head and neck, breast, lung and pancreas). Specifically, this involves growing the patient's own tumour tissues outside of the human body as tumour organoids or primary cell-line-based "avatars". These "avatars" are then screened for therapeutic and genetic vulnerabilities against a panel of drugs, including standard-of-care treatments such as chemotherapy and molecular targeted agents. Such patient-derived models can be utilised to develop patient-specific resistant and metastatic models to identify novel biomarkers that can predict tumour progression.

Using functional genomic approaches, researchers at GIS can now use these "tumour evolution models" to predict how the patient's tumour may evolve in the clinic. By being able to predict a given cancer's next evolutionary move, and identify molecular mechanisms that drive emergence of refractory disease, researchers at GIS are beginning to explore innovative therapeutic solutions that can be implemented to prevent the evolution of cancers into aggressive, malignant states.

IDENTIFYING THE GENOMIC-BASIS FOR DRUG RESPONSE AND DEVELOPING NOVEL PROGNOSTIC BIOMARKERS

Using comprehensive tumour profiling studies (mutational burden, gene expression and epigenome profiling), as well as single cell transcriptomics in conjunction with phenotypic screens, researchers at GIS are beginning to identify the genomic-basis for drug response, resistance and metastasis. Recently published studies using these methodologies have revealed specific predictive gene expression, and mutational signatures that could guide future treatment strategies validated through larger clinical trials. Successful implementation of this work can redefine how personalised medicine can be executed in the clinic, representing a paradigm shift in clinical management of the disease.

NEXT-GENERATION PLATFORMS FOR CANCER DISCOVERY: REALISING "BENCH-TO-BEDSIDE"

The battle against cancer is an evolutionary arms race. Clinicians need better and more effective drugs to treat patients. To support the goals of precision oncology, researchers at GIS are employing patient-derived tumour "avatar" models to unearth new important therapeutic targets for drug development, as well as identifying clinically approved drugs that can be repurposed for cancer therapy. The precision-medicine technology platform built by these researchers will revolutionise the way the next generation of drugs are identified and developed. We focus our goals on targeting cancer metabolism, signalling pathways, transcription and epigenetic regulators, as well as the tumour microenvironment. The discoveries made at GIS will pave the way for more effective and durable therapeutics to be added to the anti-cancer drug arsenal.

Investigators

Ramanuj **DASGUPTA**

YU Qiang

TAM Wai Leong / Sarah **NG** / Iain **TAN**

Daniel **TAN** / Elaine **LIM** / **ONG** Choon Kiat

MICROBIAL GENOMICS

GIS has a broad programme in applying genomics to the understanding and prevention of human disease. This programme spans molecular pathogenesis, pathogen genetics, disease transmission, host response, and microbiome influences. As with other GIS programmes, our human disease work is focused on improving human health and integrated with Singaporean health agencies, local and regional hospitals, and industry partners.

By their very nature, all infections involve both a host and a pathogen. A common theme of human disease research at GIS is to study host and pathogen genomics both separately as well as together, integrating to understand the interaction and dynamics that lead to host disease. We have specific expertise in bacteria, viruses, and microbiome research, with active programs in Dengue, Zika, Group B Streptococcus, urinary tract infections, the intestinal microbiome, and the skin microbiome. In one of the few molecular pathogenesis labs in Singapore for bacterial research, genomics and computational methods are integrated with *in vitro* and *in vivo* models. One unique aspect of GIS' work on human disease is the ability to perform co-development of matched experimental and computational methods to enable the simultaneous analysis of host and pathogen gene expression during *in vivo* infections.

We work closely with two technology platforms at GIS, the Scientific and Research Computing Platform (SRC) and the GERMS Platform. With SRC, we have developed custom pipelines and algorithms for analysis of pathogen genomics on our own internal compute infrastructure, emphasising the scale and integration common to all research in GIS. Looking forward, pathogen genomics is growing dramatically, driven by plummeting sequencing costs and increasing global integration. Human disease is therefore one of the leading research programmes moving to cloud computing for higher performance, faster turnaround time, and greater automation and integration.

Our progress towards broader perspectives and faster turnaround times has been invaluable as unexpected infection outbreaks arise. Learning from early lessons with SARS in 2003, GIS has continued to be the partner of choice for hospitals and public agencies in Singapore to detect, monitor, and investigate outbreaks. We have contributed expertise for nearly all recent outbreaks, including Group B Streptococcus in 2015, Zika in 2016, and several hospital outbreaks with *Staphylococcus aureus* and Group A Streptococcus. Given our unique position in Southeast Asia, we are also developing the tools and the infrastructure to proactively anticipate trends in disease and resistance as well as to prioritise other unknown and emerging infectious threats to human health.

Investigators

Swaine **CHEN**

Niranjan **NAGARAJAN**

Novel algorithms are particularly important for the rapidly developing field of microbiomes and their influence on human health and disease. Aside from common species composition pipelines, the GIS microbial genomics researchers have developed new ways to infer key community parameters, such as overall abundances, from commonly used samples and data sets. These have been applied to understand the importance of probiotics on infant nutrition and development, the role of bacterial communities on skin conditions, and the impact of and recovery from antibiotic treatment. We partner with clinical collaborators like members of the Growing Up in Singapore Towards a healthy Outcomes (GUSTO) cohort, a longitudinal case-control birth cohort of infants with rhinitis and wheeze to conduct microbial community analysis. We also collaborate with industrial partners like IBM by using other GERMS pipelines, which look at the effect of a polymer on antimicrobial resistance gene expression.

Antibiotic resistance in particular unifies many efforts of the GIS human diseases groups. From molecular genetics to rapid diagnostics, genomic detection to microbiome response, GIS spans a full spectrum of research into the rise and spread of antibiotic resistance and novel strategies for combating it. Together with our public health and hospital partners, we are actively pursuing this central challenge to Singaporean and global medicine.

COMPUTATIONAL BIOLOGY AND DATA SCIENCES

Computational Biology is at the heart of genomics. We integrate and analyse large and complex data sets in order to derive a more complete systems-level understanding of biological processes and diseases. At GIS, computational research is driven through teams that focus on the latest technology and trends in data science.

We develop state-of-the-art computational tools and pipelines for the study of a diverse range of datasets, including targeted and whole genome sequencing, transcriptome sequencing, chromatin state and transcription factor binding site profiling, metagenomics and single-cell omics. Our scientists bring together a range of expertise in biology, computer science, mathematics, and statistics to solve problems in genomic biology and medicine and collaborate closely with experimental groups working on genomic technologies, cancer, stem cells and development, human genetics and infectious diseases.

TECHNOLOGY AND LARGE-SCALE DATA

One of the key areas at GIS is the focus on computational solutions for future genomics technologies. Computational Biology and Data Sciences (CBDS) researchers have extensive experience designing methods to analyse novel datasets from cutting-edge genomic technologies such as third generation sequencing (Nanopore, PacBio), spatial transcriptomics, and single cell genomics.

In order to deal with large-scale data generated at GIS, a genome analytics core team develops fast, robust, and reproducible pipelines, incorporating the latest software releases. We utilise our local infrastructure at GIS as well as the National Supercomputing Centre and cloud computing. Through this infrastructure, groups at the Genome Institute of Singapore have contributed to national and international consortia, generating new insights into the role of the genome in human diseases.

CBDS scientists have developed provably optimal and robust algorithms for a range of problems in genomics, from ultra-fast and exact read mapping (BatMis: http://code.google.com/p/batmis/) to quality-aware rare-variant calling (LoFreq: http://sourceforge.net/projects/lofreq/), efficient, optimal algorithms for genome assembly (Opera: http://sourceforge.net/projects/operasf/, FinIS: http://sourceforge.net/projects/finis/) and optimal signal-processing of functional profiling datasets (DFilter/EFilter: http://collaborations.gis.a-star.edu.sg/~cmb6/kumarv1/dfilter/).

Investigators

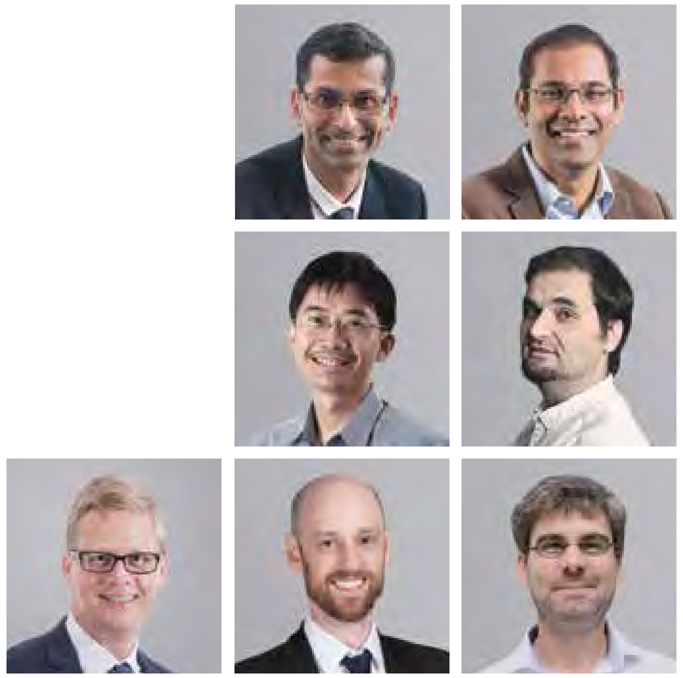
Shyam **PRABHAKAR** /
Niranjan **NAGARAJAN**

Ken **SUNG** /
Mile **SIKIC**

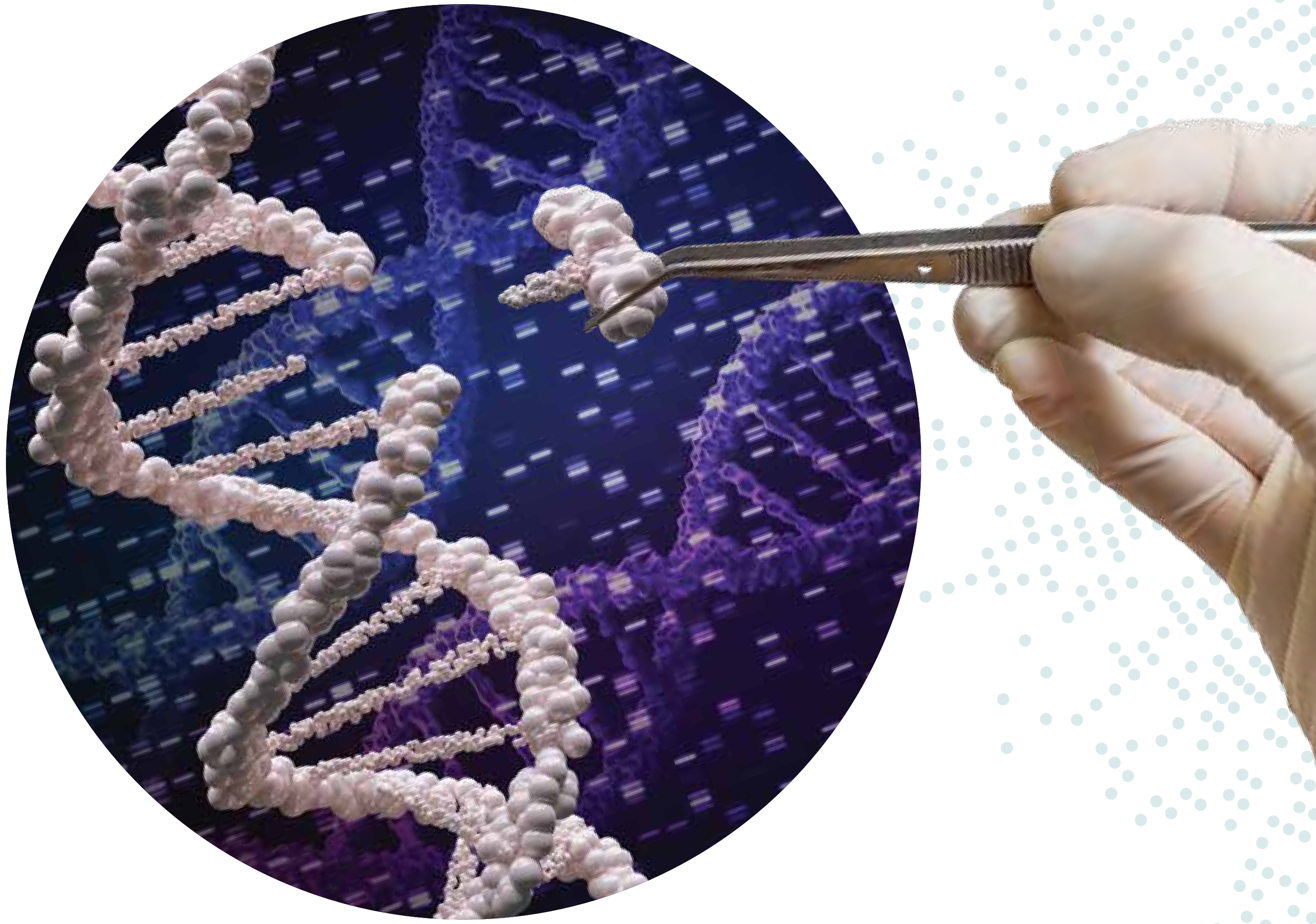
Anders **SKANDERUP** /
Jonathan **GOKE** /
Nicolas **BERTIN**

The computational tools developed at GIS are designed for a diverse array of questions in genomic medicine, including the following central themes in the CBDS programme:

- How can genomics technology and data science help to improve health care?
- What is the role of non-coding sequences in the human genome?
- How can we identify and characterise disease-causing non-coding mutations?
- What is the molecular and genetic basis of human diseases?
- Can patient-specific driver mutations be predicted and used to personalise cancer therapy?
- What is the role of microbial communities in the human body in health and disease states?



GENOMIC TECHNOLOGIES



Investigators

WAN Yue
TAN Meng How
Sho **GOH**
Niranjan **NAGARAJAN**

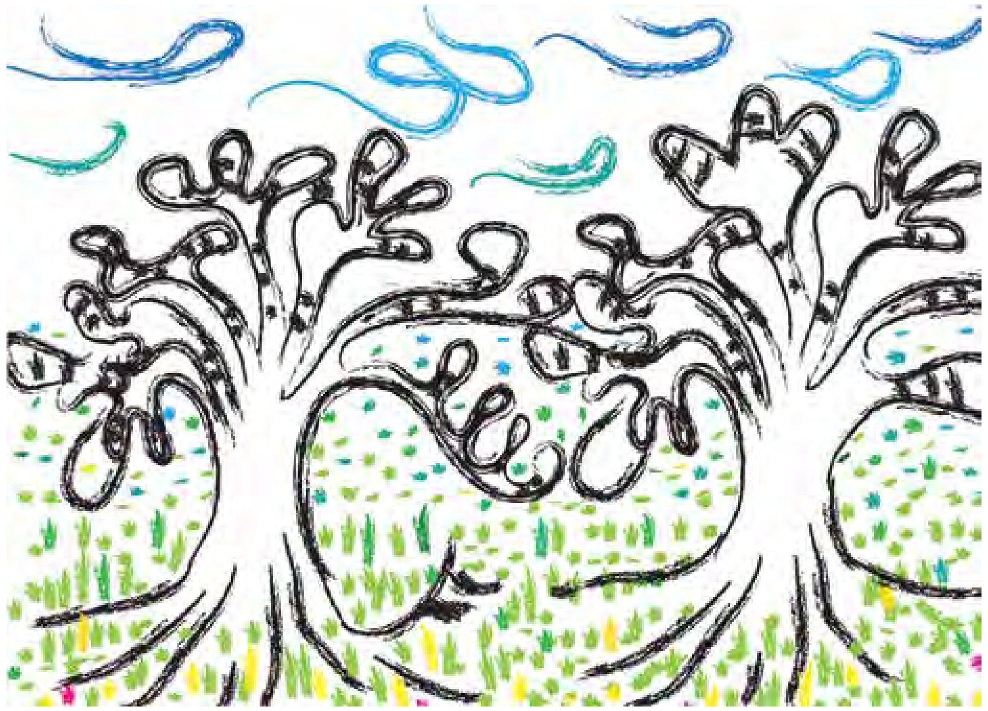
RNA TECHNOLOGIES

The Genome Institute of Singapore has a strong programme on studying RNA and its diverse processes. The programme studies RNA beyond its primary sequence and utilises high throughput technologies to study RNA structure, RNA editing and RNA modifications in different diseases. This extends outside of the traditional view of targeting DNA and aims to understand and utilise the properties of RNA as a potential drug target.

The GIS RNA programme is also integrated with Singapore health agencies and other institutions and universities to improve human health.

While much effort has been focused in the last decade on studying how DNA and protein contribute to gene regulation, recent studies have shown that RNA plays important roles in almost every cellular process. Beyond its primary sequence, RNA can fold into complex secondary and tertiary structures, and are extensively processed and modified in diverse cellular functions. Errors in post-transcriptional processes such as folding, alternative splicing and RNA editing can result in the development of cancer and neurological disorders. We aim to utilise and develop high throughput technologies to study how RNAs work inside cells, in order to target RNA for disease treatment.

Colourful structural landscapes of transcriptomes in human cells. – Designed by Dr WAN Yue



We work closely with several technology platforms in GIS, including the Genome Analytics Core, High Throughput Sequencing Platform, GERMS Platform and the Genome Innovation Laboratory. In collaboration with other computational groups within GIS, we develop novel analysis tools to study new datasets on RNA function. We also collaborate with other biology groups within GIS to study RNA under different developmental and disease processes. This extensive network of interactions has enabled us to develop new technologies to study how RNAs interact with other molecules globally, as well as how they could be regulated through RNA editing.

By continuing to develop and apply new technologies, we hope to discover new functions in this major class of macromolecules in diseases to facilitate better treatment.

CRISPR AND NUCLEIC ACID EDITING

The Genome Institute of Singapore is rewriting life. We do this by developing the most exciting technologies to massively change DNA in human genes, correcting the root causes of diseases, and synthesising new genomes from scratch.

Our work contributes to what has been called 'the biggest biotech discovery of the century' by the MIT Technology Review - the CRISPR-Cas technologies. At GIS, our work is pushing the limits of CRISPR-Cas technologies for genome (DNA) and transcriptome (RNA) engineering.

New CRISPR-Cas advances enable the creation of genetic change faster, better, and cheaper than ever before. These breakthroughs open up compelling avenues to directly remedy disease-causing genes. Combined with the ease of massive parallelisation, we now dissect entire genomes letter-by-letter, so as to illuminate disease vulnerabilities, drug modes of action, and combat viruses.

Investigators

CHEW Wei Leong
TAN Meng How

We further engineer the Cas protein with novel function-conferring effector domains that include transcription regulators, epigenetic regulators, fluorescent proteins, and deaminases, each of which allows us to create a unique functional change to the genetic location of choice.

Together, these multiple applications of CRISPR-Cas underscore its widespread utility, and promise a future of new diagnostics and medicines. At GIS, we continue to unlock the full potential of CRISPR-Cas technology by resolving the most outstanding obstacles impacting its use. Our work is making CRISPR-Cas more potent, more specific, more broadly applicable, easier to use, and safer. In doing so, we are inventing the new generation of research tools and molecular therapeutics.

Our work is part of a future where new life forms are created from the most fundamental building blocks. We develop new molecular machines that read, write, assemble, and repair DNA, so that we can engineer life direct from design. We interface the biological with the physical so that we can interconvert binary instructions with DNA sequences. We generate mini human organs harbouring new genetic blueprints. We build living things from imagination.

These technologies dramatically impact our future in how we rapidly combat disease outbreaks, manufacture biologics and medicines, disseminate cures, realise our imagination, and answer the hardest questions in what defines life. The Genome Institute of Singapore develops these cutting-edge technologies to answer these most pressing challenges facing our world.

LIQUID BIOPSY

Liquid biopsy refers to a non-invasive diagnostic test or technology that can identify conditions related to the tumour by detecting biomarkers in fluid samples such as blood or urine. This is different from traditional tissue biopsy which uses tumour tissues to serve a diagnostic purpose. As fluid samples, mainly blood of cancer patients, can be routinely and easily obtained from cancer patients, it has the potential to revolutionise cancer management by providing real-time monitoring and diagnosis of tumour. Liquid biopsy is gaining widespread interest in the area of cancer research and diagnosis, where genomic alterations have been shown to drive tumour progression and influence tumour response to treatment therapy.

Cancers accumulate genomic alterations as the tumour progresses. With the development of large-scale biologic databases, powerful technologies for patient characterisation and computational tools for big data analysis, the majority of the driver oncogenes have been uncovered. As we move into the era of precision medicine or individualised treatment therapy based on biologic behaviour of tumour, liquid biopsy, which has the ability to diagnose tumour and monitor its progression without the need to obtain tissue biopsy, is becoming one of the most exciting developments in cancer management.

At GIS, we use a wide variety of advanced, contemporary technology platforms to detect ultra-low frequency genomic alterations from the blood of cancer patients. We work with various national hospitals and clinics to discover novel blood-based biomarkers from cancer patients which can be used for clinical applications such as disease monitoring, prognosis and evaluation of therapy response.

Most recently, we have identified a novel blood-based biomarker strongly associated to breast cancer relapse. Our team at GIS is developing a liquid biopsy blood-based assay to detect circulating tumour DNA, which can potentially be used in the clinic to identify high risk relapse patients, monitor treatment response, as well as a companion diagnostic for future drugs.

GIS is also actively involved in the national liquid biopsy programme (**CaLiBRe**: **Ca**ncer **Li**quid **B**iopsy for **Re**al-time diagnostics and early intervention) to profile the blood of cancer patients from diagnosis to relapse, in order to identify emerging genomic alterations as early as possible. We aim to develop innovative liquid biopsy genomics assays which can be implemented in the clinics to benefit cancer patients. With our CAP (College of American Pathologists)-accredited facilities, we have the complete framework to develop and validate our research discoveries into functional liquid biopsy assays for clinical applications.

Investigators

YU Qiang
Sarah **NG**
Iain **TAN**

Investigators

CHEN Kok Hao
Shyam **PRABHAKAR**
LIU Jinyue



SPATIAL TRANSCRIPTOMICS

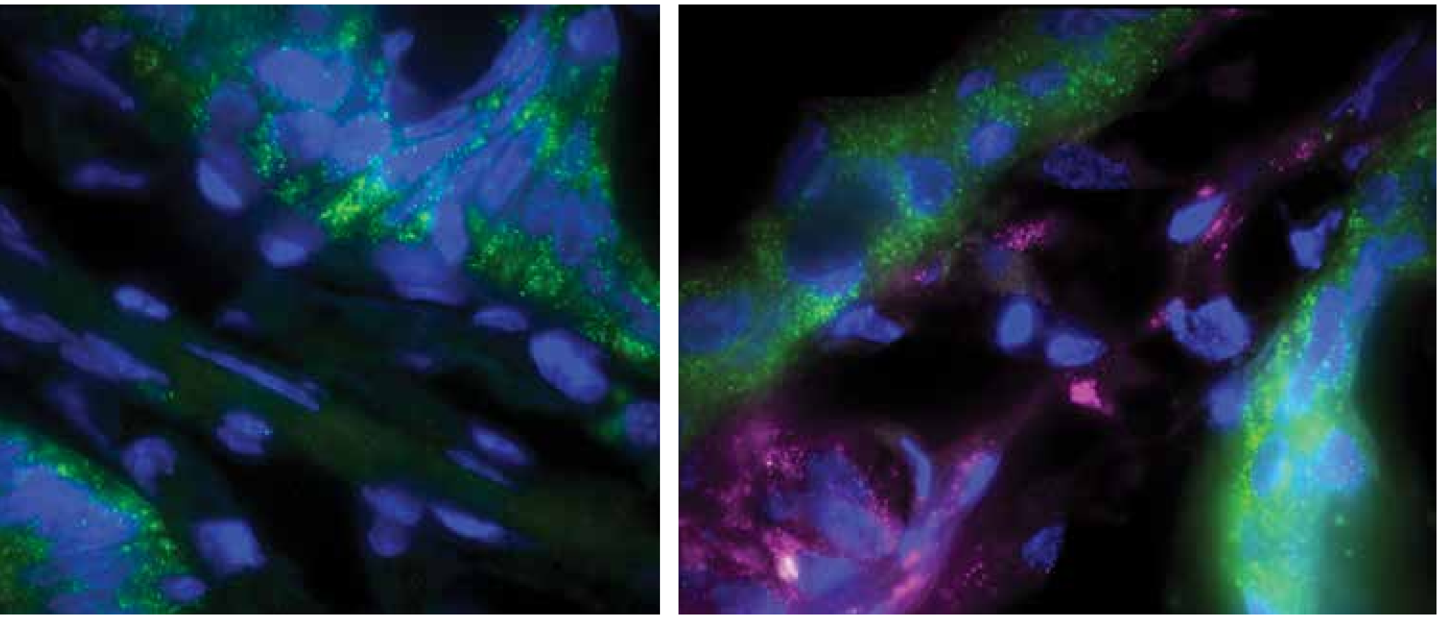
The transcriptome of a cell contains a wealth of information about the cell's current state as well as its recent history. An individual's stem cells, skin cells, and neurons all have the same genome, but differ in their gene expression profile.

While next-generation sequencing is a powerful technology that can reveal the complexity of the human transcriptome, transcripts analysed need to be extracted from tissues, thus destroying their native spatial relationships. Yet, the tissue context of gene expression is of tremendous biological importance – most physiological processes take place under intricate cellular coordination and proper cell-cell interactions are vital for tissue health. If we can map the transcriptome of all the cells from an intact tissue, we can examine, at the most fundamental level, how different cell types in the mammalian tissues work together.

Multiplexed fluorescence in situ hybridisation (FISH) is an attractive approach for spatial transcriptomics (ST), and has recently been implemented under various schemes, such as cyclic single-molecule FISH (smFISH), sequential FISH (seqFISH), and multiplexed error-robust FISH (MERFISH). In particular, we showed that MERFISH can be used to spatially image hundreds to thousands of RNA species within single cells.

Currently, laboratories in GIS are interested to develop new ST technologies and apply them to answer questions in both healthy and pathological tissues.

Drug-induced stem-cell switch (from Sox2 to Sox9) activates epigenetic re-programming driving tumor evolution in squamous cell carcinomas.



TRANSLATIONAL RESEARCH

The Translational Research Group at GIS promotes the smooth transition from basic research to advances in science and technology, and hence, to innovation. The group mainly focuses on molecular diagnostics. Our mission is to provide and market molecular diagnostic discoveries aligned with industry needs, as well as to further develop these together with commercial partners.

With the ability to develop diagnostics for all assay formats and disease areas, the group can provide strong evidence that newly discovered biomarkers can be a significant tool for personalised patient care. We are equipped with the most advanced technology platforms necessary for research and development in genomics, and application of genomic techniques to biological and medical questions.

In order to achieve major aims, there was a need for a proper Molecular Diagnostics Lab (MDx) and experience in engaging industries. Therefore, a Molecular Diagnostics Laboratory was designed and constructed in compliance to ISO 13485 (an internationally recognised standard for the commercialisation of medical devices) workflow requirements. It was subsequently certified and accredited by TÜV Rheinland in December 2014.

The MDx was the first lab in GIS to achieve certification, allowing the institute to position itself as a preferred partner for strategic collaborations with Biotech, Pharma and hospitals. With steady support to the various GIS research groups through assay development, optimisation and validation in regulated environment, it significantly shortens the distance to clinical applications.

Investigators

Alexander **LEZHAVA**
TAN Yann Chong
Astrid **IRWANTO**
Justin **TAN**
Oliver **WORSLEY**





PLATFORM

TECHNOLOGIES

The Genome Institute of Singapore has a wide range of technologies used in modern genomic and cellular biology investigations. Advanced research methods, and the dedicated equipment designed to perform these methods, allow for new approaches to tackle challenging and new biological questions, opening up new vistas for exploration. With our technology platforms, we support genomics research across multiple A*STAR institutes, universities, hospitals, industries as well as international partners.

Investigators

KHOR Chiea Chuen
Next Generation Sequencing
Genotyping

Giridharan **PERIYASAMY**
High Throughput Phenomics

NEXT GENERATION SEQUENCING

Established over a decade ago, the GIS Next Generation Sequencing Platform has evolved to become the largest and most productive academic sequencing facility in Singapore. GIS' team of scientists also developed the first protein-mediated interactome protocol, ChIA-PET. As an endpoint service to a wide range of applications that answer different biological questions, the sequencing platform is critical to the ability to generate data from whole genome sequencing to RNA-sequencing, ChIP-sequencing, exome sequencing and more.

With a fleet of Illumina HiSeq and PacBio sequencers, the platform generates massive amounts of data – up to 150 teraBytes or 200 gigabases per year. These include 400 million reads per flowcell, in as short as a one-day turnaround. This state-of the-art sequencing platform is constantly updating itself with the newest technologies, to maintain its top spot as a sequencing service in Singapore. Not only does the platform look to produce reliable sequencing data in a high throughput manner, it is also expanding its capabilities with new machines to produce longer reads and allow miniaturised sample preparations.

Besides housing the newest and most capable sequencers, the sequencing group also automates parts of the process with liquid handlers.

GENOTYPING

High throughput, next generation genomic technologies are revolutionising the manner in which research in the field of human heredity is being carried out. As a national institute for genetic and genomic research, sustaining capability and high-level expertise in these technologies is a key strategic priority of GIS in maintaining its position as one of the leading research institutes in the field.

Being the national flagship institute for genomic research in Singapore, we specialise in a very broad selection of array technology from Illumina and Affymetrix to empower our discovery efforts into the underlying genetic causes of human diseases (both common and rare). We also undertake focused genotyping using the Sequenom and Taqman systems for validation purposes. With dedicated automation and quality control pipelines, we support a wide range of experimental protocols for human genetic research.

We aim to bring together genomics and analysis services to support practising clinicians and scientists from both Singapore and abroad wanting to leverage on the latest technologies in genomics for their research. We collaborate with GIS multi-disciplinary research teams in human genetics, cancer biology and stratified oncology, stem cells, and with researchers across America, Asia and Europe.

HIGH THROUGHPUT PHENOMICS

The Centre for High Throughput Phenomics (CHiP) Platform aims to provide an integrated, state-of-the-art, functional and chemical genomics-based high-throughput/high-content screening (HTS/HCS) platform in Singapore.

High Throughput Screening (HTS) has transformed the way biomedical research is performed by employing laboratory automation and robotics, enabling the functional interrogation of the entire genome and identification of therapeutic drug candidates in a much shorter timeframe than earlier. The application of HTS/HCS will ultimately enable the practice of targeted treatments, a first step towards Personalised Medicine.

The CHiP-GIS has been established as a shared resource for the application of functional and chemical genomic technologies to support the research programs of investigators at GIS and beyond. In doing so, the CHiP-GIS hopes to bring together research scientists, ideas and technologies from all aspects of biomedical research in academia, the clinic and industry.

GIS EFFICIENT RAPID MICROBIAL SEQUENCING (GERMS)

Our pathogen sequencing infrastructure (termed the GERMS Platform) is dedicated to all microbial sequencing: viral, bacterial, fungal, and parasitic. Our standard analyses include microbiome (both 16S and metagenomics), whole genome sequencing, transcriptomics, and population diversity analyses (such as for viral populations within a single infected individual); custom analyses are also available. The GERMS Platform has many active collaborations both in Singapore and internationally, which include academic, government, and industrial partners. GERMS offers a complete package for microbial genomics, from project design to sample handling, sequencing, analysis, and interpretation.

COMPUTATIONAL PHENOMICS

The Computational Phenomics Platform (CPP-GIS) provides comprehensive computational support for research and exploration involving functional and chemical genomics-based High-Throughput/High-Content Screening (HTS/HCS). We focus on the development of analysis tools and novel descriptors for complex phenotypes (morphological features) to facilitate drug/therapeutic discovery and functional genomic studies linked to phenotypical outcomes, with important implications in the treatment of human diseases including cancer, neurodegenerative diseases and diabetes.

With a spectrum of expertise in high content image analysis, database development, Artificial Intelligence/machine learning, and system biology/network interference, and through a strong partnership with the CHiP-GIS Platform, industry and clinical advocates, CPP-GIS is dedicated to the discovery of biologically relevant molecular probes, novel diagnostic and therapeutic avenues contributing to research programmes and industry partnerships on precision oncology, drug discovery and functional genomics in Singapore and beyond.

Investigator

Judice **KOH**
Computational Phenomics

Investigators

Shyam **PRABHAKAR**
Single Cell Genomics
C-BIG

Ramanuj **DASGUPTA**
Single Cell Genomics

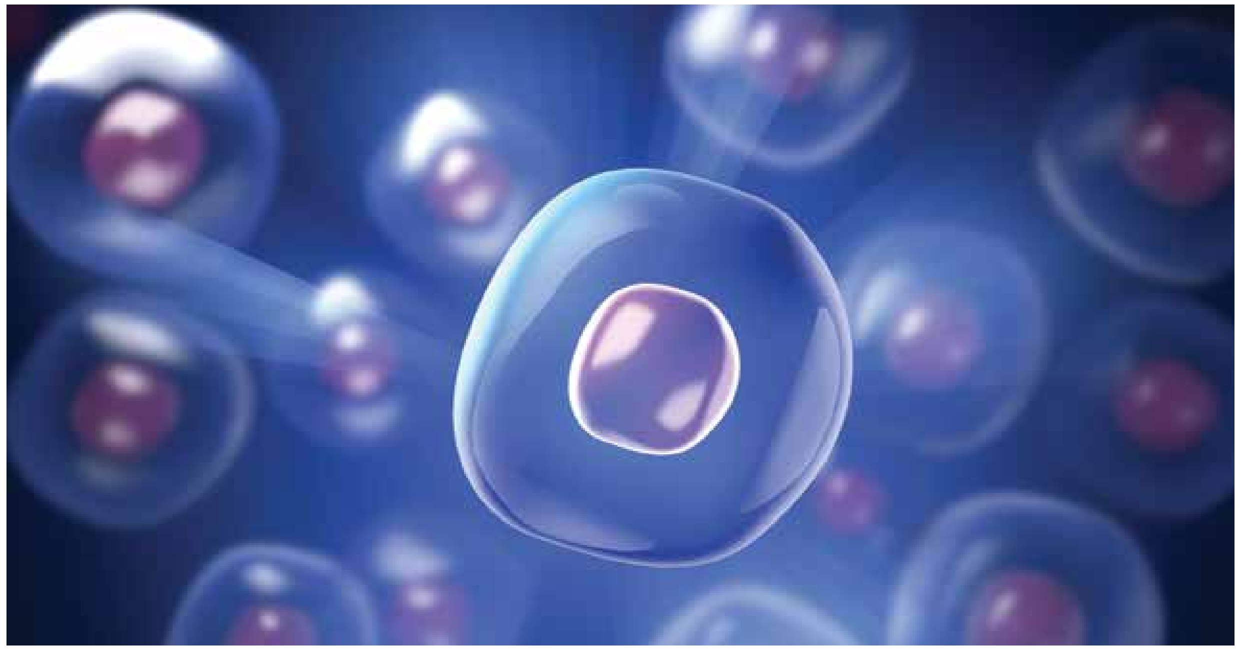
Roger **FOO**
Single Cell Genomics
FOO Jia Nee
Single Cell Genomics

LIU Jian Jun
Single Cell Genomics
CHEW Wei Leong
Single Cell Genomics

SINGLE CELL GENOMICS

The GIS Single-Cell Omics Centre (SCOC) is a laboratory located within the Institute dedicated to accelerating the understanding of how individual cells work, and how diagnosis and treatment might be enhanced through insight derived from single cells.

The mission of the SCOC is based on the concept that the cell is the basic building block of life. The human body is composed of billions of individual cells representing thousands of cell-types all intricately communicating with one another. One of the goals of this Centre is to define biological systems at this level, whether in diseased states or normal development, by analysing the transcriptomes and genomes of individual cells. By profiling the transcriptome of many individual cells within a population, one gains unparalleled insight into the diversity of cell types and how they communicate among themselves. Such a level of understanding provides mechanistic insights into how cells self-renew, differentiate, evolve (both between species and within cancers), and respond to infection and/or drug treatments. The Centre allows access to cutting-edge single-cell genomics technologies including 10x Genomics, WaferGen and Fluidigm.



The Centre features 10x Chromium controller produced by 10x Genomics which allows efficient processing of thousands of single cells for multiple downstream applications. The 10x Chromium system enabled applications include single cell gene expression, single cell immune profiling, whole genome/exome sequencing, single cell CNV and single cell ATAC-seq. The Centre is also equipped with WaferGen ICELL8™ Single-Cell System, which allows single cell mRNA sequencing and image acquisition of captured cells.

The Centre also features advanced microfluidic technologies produced by Fluidigm enabling single cell transcriptomics and genomics. Equipment within the Centre includes two C1™ Single-Cell Auto Prep Systems, which automatically capture individual cells from small tissue quantities. The nucleic acids produced on this system and generated from individual cells can subsequently be analysed by high throughput real-time PCR on the two Fluidigm BioMark™ HD Systems housed in the Centre or by NextGen sequencing machines located within GIS.

CENTRE FOR BIG DATA AND INTEGRATIVE GENOMICS (C-BIG)

The Centre for Big Data and Integrative Genomics (c-BIG) is a multi-institutional effort hosted in part in GIS. It was established in 2016 to enable big data analytics and integrative genomics in Singapore. Its core mission is two-fold : (i) provide data infrastructure to large-scale industry and A*STAR-supported clinical research projects in Singapore and (ii) provide state-of-the-art pipelines for sequencing-based research and support for clinical units lacking sufficient analytics capabilities. c-BIG's current flagship projects include population-scale genomic data governance and analytics for the SG10K and the National Precision Programme.

GENOME INNOVATION

The Genome Innovation Laboratory is a platform built on the theme of making genomics accessible. We provide services to test, optimise and run genomics protocols, especially those that utilise high-throughput sequencing as a readout. Our particular interests are in up-and-coming, novel approaches. Working closely with clinicians, researchers and the GIS Next Generation Sequencing Platform, we aim for broad coverage of genomic technologies with high quality results. Our recent projects include techniques for sensitive variant detection in the context of liquid biopsies, as well as being a testbed for long-read sequencing using Nanopore technologies.

GENOME ANALYTICS CORE

The GIS Genome Analytics Core Platform provides efficient genome analytics capabilities that modern genomics research builds upon. Rapid advances in genome sequencing technologies and the exponential growing data throughput make scalable analytics and data management solutions critical. By providing these services, the Genome Analytics Core Platform enables researchers to focus on the science, rather than details of computational platforms and systems.

The platform has access to a variety of high-performance compute platforms, including an in-house cluster with petabyte-scale storage, the National Supercomputing Centre (NSCC) Singapore, as well as leading public cloud service providers with data centres in Singapore. This hybrid compute environment allows the platforms to deliver the most efficient solutions to researchers.

The platform is embedded within GIS and can thus leverage on the scientific expertise of in-house computational research groups and is closely aligned with the scientific goals behind analytics. The platform is further tightly integrated into national programmes, for example, the National Precision Medicine Programme.

Leveraging on open community and industry standards, the platform provides integrated and end-to-end solutions from raw genomic data to custom analytics and applications. As of 2018 primary and secondary analysis services are offered to the wider community through the Integrated Genomics Analytics Platform (iGAP).

Investigators

Nicolas **BERTIN**
C-BIG

Sarah **NG**
C-BIG
Genome Innovation

SHIH Chih Chuan
C-BIG
Genome Analytics Core

PARTNERSHIP PROGRAMME

To enrich its research programmes and to build a broader national framework for the genomic sciences, the institute launched the GIS Partnership Programme in 2013. The programme consists of associate faculty who bring complementary research strengths to the core faculty of GIS and help to build up new areas of research. Through a close partnership between the core and associate faculty, this collective group synergises to direct and expand the GIS science portfolios. The associate faculty members are closely engaged in the scientific agendas of GIS, and help to enhance the GIS Translational and Clinical Research (TCR) profile and expand the GIS collaborative network.

•••

Professor TEH Bin Tean is Deputy Director (Research) at the National Cancer Centre and Deputy Director (Global Relations) at the SingHealth Duke-NUS Institute of Precision Medicine. He is also Professor at Duke-NUS Medical School and Senior Principal Investigator at Cancer Science Institute of Singapore, as well as Institute of Molecular and Cell Biology. His main research focus is on translational cancer research.

•••

Associate Professor DAN Yock Young is the Chair of University Medicine Cluster, NUHS and the Head of Department of Medicine, NUS. He is also Senior Consultant at Division of Gastroenterology and Hepatology and Adjunct at Cancer Science Institute. His research focus includes cost effectiveness of clinical treatment, liver stem cells and their therapeutic applications, liver cancer as well as fatty liver and metabolic liver disease.

•••

Professor Pierce CHOW Kah Hoe is Professor and Course Director at Duke-NUS Medical School; Senior Consultant and Co-Director (Surgical) of the Comprehensive Liver Cancer Clinic at the National Cancer Centre Singapore; and Senior Consultant Surgeon in HPB and Transplant Surgery at the Singapore General Hospital. He leads the Program in Clinical and Translational Liver Research at the National Cancer Centre and is Protocol Chair of the Asia-Pacific Hepatocellular Carcinoma Trials Group. His research interests are in hepatocellular carcinoma and steato-hepatitis.

•••

Professor TAN Boon Ooi Patrick is Executive Director of GIS; Professor of Cancer and Stem Cell Biology at Duke-NUS Medical School; Director, SingHealth Duke-NUS Institute of Precision Medicine; Senior Principal Investigator at Cancer Science Institute of Singapore (NUS); Director at Duke-NUS Genome Biology Facility; Principal Investigator (Adjunct) at National Cancer Centre, Singapore; and Professor (Adjunct), Department of Physiology at National University of Singapore. His research focuses on developing genomic approaches to unlock the molecular and clinical diversity of gastric cancer.

•••

Adjunct Associate Professor LEONG Khai Pang is Senior Consultant (Rheumatology, Allergy and Immunology) at Tan Tock Seng Hospital. His research focus are rheumatology and personalised medicine.

•••

Associate Professor ONG Sin Tiong is an Associate Professor in the Cancer & Stem Cell Biology Programme at the Duke-NUS Medical School in Singapore. He is a haematologist and a medical oncologist. His research foci are translational in nature, and centre on gaining a better understanding of the mechanisms which gave rise to cancer drug resistance, and defining novel therapeutic strategies to overcome drug resistance.

•••

Professor Martin Lloyd HIBBERD is Professor of Emerging Infectious Disease London School of Hygiene and Tropical Medicine; and Co-Founder and Director of PathGENDx, a GIS spin-out company. He started in GIS in January 2003 and was the Senior Group Leader of the Infectious Diseases laboratory. In April 2017, under the GIS partnership programme, he was appointed as the Associate Faculty member. His research interest covers both pathogen and host aspects of infectious disease, understanding how microbial agents causes the observed disease and why specific individuals are susceptible to the disease.

•••

Professor Mark RICHARDS is Director of the Cardiovascular Research Institute, National University Health System, and Director of the Cardioendocrine Research Group (CCERG; now re-named the Christchurch Heart Institute), University of Otago. From 1987, Prof Richards has coordinated integrated programmes of research incorporating the disciplines of clinical applied research, cardiovascular peptide biochemistry, molecular biology and preclinical physiology.

•••

Professor Tin AUNG is Executive Director at the Singapore Eye Research Institute (SERI) and Senior Consultant, Glaucoma Department and Deputy Medical Director (Research) of the Singapore National Eye Centre (SNEC). He is also a full tenured Professor with the Department of Ophthalmology, National University of Singapore and Kwan Im Thong Hood Cho Temple Professor of Ophthalmology, Duke-NUS Medical School, Singapore. Prof Aung is a clinician-scientist and leads the Glaucoma Research Group at SNEC/SERI. His main research interests are angle closure glaucoma and molecular genetics of eye diseases.

•••

Professor Bernhard BOEHM is Professor of Metabolic Medicine at the Lee Kong Chian School of Medicine, Nanyang Technological University, and Deputy Director (Clinical) of NTU Institute for Health Technologies. He is also Senior Consultant, Endocrinology, Tan Tock Seng Hospital, Singapore. Prof Boehm has made seminal contributions in the field of diabetes and metabolic medicine. Prof Boehm was Director of a National Institutes of Health (USA) funded European biobank, which stores samples from over 1,500 multiplex diabetes families.

•••

Professor TEO Yik Ying is Dean of the Saw Swee Hock School of Public Health, National University of Singapore, and concurrently the iOmics Programme Leader at the Life Sciences Institute, and an Associate Faculty Member of GIS. Prof Teo majored in statistical genetics and has gained international recognition for his work in genomics, where his focus is in the development and application of mathematical and statistical techniques to understand the genetic causes of human diseases and genetic evolution in worldwide populations.

•••

Professor TAI E Shyong is a Professor in the Department of Medicine at the Yong Loo Lin School of Medicine, National University of Singapore, the Saw Swee Hock School of Public Health and Duke-NUS Graduate Medical School. Dr Tai has a longstanding interest in the development of novel treatments for diabetes mellitus that leverages on human genetics for the identification of novel drug targets. More recently, he has begun working on better ways to implement existing treatments into clinical practice to optimise cost effectiveness.

•••

Professor Edward KOO is Professor at the Department of Medicine and Physiology at the Yong Loo Lin School of Medicine, National University of Singapore and Professor at the Department of Neurosciences at the University of California, San Diego School of Medicine. His lab focuses on understanding the molecular and cellular pathophysiology of Alzheimer's disease. He has been recognised for studies on -secretase modulators, their mechanism of action and potential as Alzheimer's disease therapy; in characterising the processing and trafficking pathways of APP and amyloid production as well as in physiological functions of APP that are amyloid independent; and more recently, on synaptic injury in Alzheimer's disease.

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Professor Stuart COOK is Director at the National Heart Research Institute Singapore, Senior Consultant at the National Heart Centre Singapore, Professor of Clinical and Molecular Cardiology at Duke-NUS, and Professor of Clinical and Molecular Cardiology at Imperial College. He heads a cross-disciplinary research team, anchored in human genetic discoveries, with the overarching goal of identifying new genes and pathways for heart disease to reveal new biology and therapeutic targets. Prof Cook's research focus is on genetic basis of cardiovascular disease, disease mechanisms, CMR, novel diagnostics, therapeutic target development, ICCs and heart failure.

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Professor WONG Tien Yin is Provost's Chair Professor of Ophthalmology and Medical Director at the Singapore National Eye Centre, and Chairman of SNEC's research division. Prof Wong is also Vice Dean, Office of Academic & Clinical Development at the Duke-NUS Medical School. Since January 2018, he was appointed Deputy Group Chief Executive Officer (Research and Education), SingHealth. In his clinical and research role, Prof Wong is a retinal specialist. He leads a broad-based research programme comprising epidemiological, clinical and translational studies of Asian eye diseases, particularly retinal diseases, and on the use of retinal imaging to predict disease risk.

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Professor TAN Eng King is a senior consultant neurologist and clinician scientist at the Singapore General Hospital, National Neuroscience Institute (NNI), a Professor at Duke-NUS Medical School and an honorary Professor at Lee Kong Chian School of Medicine. He is the Director of Research at NNI and Principal Investigator of the Neurogenetics laboratory. Prof Tan specialises in movement disorders and his primary research interests are in genetic epidemiology and the molecular mechanism underpinning disease causing genes in Parkinson's disease and essential tremor. He is also actively engaged in clinical trials, neuroimaging, quality of life and pharmacogenetic studies in various neurological diseases.

RESEARCH ADMINISTRATION

The Research Administration division of GIS is the institute's supporting arm. Not unlike the oil that lubricates the engine, the main function of the division is to ensure the smooth-running of the scientific research activities of the institute.

To this end, the various offices within Research Administration work intimately with internal colleagues and external publics. Together, Research Administration and the scientific domains and platforms form an integral network of functions that serve to promote, enhance and engineer a healthier lifestyle.

The GIS Research Administration comprises the following offices:

- Academic Affairs
- Corporate Communications
- Facilities / Safety
- Finance
- Grant Management
- Human Resources
- Procurement and Contracts
- Research Planning and Management
- Strategic Alliances and Knowledge Management

KEY REPRESENTATIVE PUBLICATIONS

Aung T, Ozaki M, Lee MC, Schlötzer-Schrehardt U, Thorleifsson G, Mizoguchi T, Igo RP Jr, Haripriya A, Williams SE, Astakhov YS, Orr AC, Burdon KP, Nakano S, Mori K, Abu-Amero K, Hauser M, Li Z, Prakadeeswari G, Bailey JNC, Cherecheanu AP, Kang JH, Nelson S, Hayashi K, Manabe SI, Kazama S, Zarnowski T, Inoue K, Irkec M, Coca-Prados M, Sugiyama K, Järvelä I, Schlottmann P, Lerner SF, Lamari H, Nilgün Y, Bikbov M, Park KH, Cha SC, Yamashiro K, Zenteno JC, Jonas JB, Kumar RS, Perera SA, Chan ASY, Kobakhidze N, George R, Vijaya L, Do T, Edward DP, de Juan Marcos L, Pakravan M, Moghimi S, Ideta R, Bach-Holm D, Kappelgaard P, Wirostko B, Thomas S, Gaston D, Bedard K, Greer WL, Yang Z, Chen X, Huang L, Sang J, Jia H, Jia L, Qiao C, Zhang H, Liu X, Zhao B, Wang YX, Xu L, Leruez S, Reynier P, Chichua G, Tabagari S, Uebe S, Zenkel M, Berner D7, Mossböck G, Weisschuh N, Hoja U, Welge-Luessen UC, Mardin C, Founti P, Chatzikyriakidou A, Pappas T, Anastasopoulos E, Lambropoulos A, Ghosh A, Shetty R, Porporato N, Saravanan V, Venkatesh R, Shivkumar C, Kalpana N, Sarangapani S, Kanavi MR, Beni AN, Yazdani S, Lashay A, Naderifar H, Khatibi N, Fea A, Lavia C, Dallorto L, Rolle T, Frezzotti P, Paoli D, Salvi E, Manunta P, Mori Y, Miyata K, Higashide T, Chihara E, Ishiko S, Yoshida A, Yanagi M, Kiuchi Y, Ohashi T, Sakurai T, Sugimoto T, Chuman H, Aihara M, Inatani M, Miyake M, Gotoh N, Matsuda F, Yoshimura N, Ikeda Y, Ueno M, Sotozono C, Jeoung JW, Sagong M, Park KH, Ahn J, Cruz-Aguilar M, Ezzouhairi SM, Rafei A, Chong YF, Ng XY, Goh SR, Chen Y, Yong VHK, Khan MI, Olawoye OO, Ashaye AO, Ugbede I, Onakoya A, Kizor-Akaraiwe N, Teekhasaenee C, Suwan Y, Supakontanasan W, Okeke S, Uche NJ, Asimadu I, Ayub H, Akhtar F, Kosior-Jarecka E, Lukasik U, Lischinsky I, Castro V, Grossmann RP, Megevand GS, Roy S, Dervan E, Silke E, Rao A, Sahay P, Fornero P, Cuello O, Sivori D, Zompa T, Mills RA, Souzeau E, Mitchell P, Wang JJ, Hewitt AW, Coote M, Crowston JG, Astakhov SY, Akopov EL, Emelyanov A, Vysochinskaya V, Kazakbaeva G, Fayzrakhmanov R, Al-Obeidan SA, Owaidhah O, Aljasim LA, Chowbay B, Foo JN, Soh RQ, Sim KS, Xie Z, Cheong AWO, Mok SQ, Soo HM, Chen XY, Peh SQ, Heng KK, Husain R, Ho SL, Hillmer AM, Cheng CY, Escudero-Domínguez FA, González-Sarmiento R, Martinon-Torres F, Salas A, Pathanapitoon K, Hansapinyo L, Wanichwecharugruang B, Kitnarong N, Sakuntabhai A, Nguyn HX, Nguyn GTT, Nguyn TV, Zenz W, Binder A, Klobassa DS, Hibberd ML, Davila S, Herms S, Nöthen MM, Moebus S, Rautenbach RM, Ziskind A, Carmichael TR, Ramsay M, Álvarez L, García M, González-Iglesias H, Rodríguez-Calvo PP, Cueto LF, Oguz Ç, Tamcelik N, Atalay E, Batu B, Aktas D, Kasım B, Wilson MR, Coleman AL, Liu Y, Challa P, Herndon L, Kuchtey RW, Kuchtey J, Curtin K, Chaya CJ, Crandall A, Zangwill LM, Wong TY, Nakano M, Kinoshita S, den Hollander AI, Vesti E, Fingert JH, Lee RK, Sit AJ, Shingleton BJ, Wang N, Cusi D, Qamar R, Kraft P, Pericak-Vance MA, Raychaudhuri S, Heegaard S, Kivelä T, Reis A, Kruse FE, Weinreb RN, Pasquale LR, Haines JL, Thorsteinsdottir U, Jonasson F, Allingham RR, Milea D, Ritch R, Kubota T, Tashiro K, Vithana EN, Micheal S, Topouzis F, Craig JE, Dubina M, Sundaresan P, Stefansson K, Wiggs JL, Pasutto F, Khor CC. “Genetic association study of exfoliation syndrome identifies a protective rare variant at LOXL1 and five new susceptibility loci.” *Nat Genet.* 2017;49(7):993-1004

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TRAINING OPPORTUNITIES

The Genome Institute of Singapore provides an excellent training ground for developing research and professional skills essential to a successful career as a scientist. The multi-disciplinary environment at GIS exposes young scientists to a range of biological, technological and computational expertise that are used to tackle some of the most pressing questions in human health.

FELLOW PROGRAMMES

The goal of the GIS Fellow programmes is to groom a cadre of early career researchers working in translational and/or strategic research areas for the next phase of Genomics Sciences.

The strategic research areas include:
① Genomic Medicine
② Precision Oncology
③ Infectious Diseases
④ Genomic Technologies (RNA Technologies, CRISPR and Nucleic Acid Editing, Liquid Biopsy and Spatial Transcriptomics)
⑤ Computational Biology and Data Sciences

The programmes provide exceptionally talented and promising new PhD and/or MD/M.B.B.S. graduates the opportunity to set up and run their research projects as a GIS Fellow or GIS Clinician Scientist (CS) Fellow. They will receive mentoring from the faculty they interact with and will be hosted in a laboratory of their choice. They will be given financial support, space and resources in a nurturing environment with access to state-of-the-art research facilities.

GIS FELLOW

The GIS Fellow programme is geared to the accomplished PhD graduate that has a vision of the science he/she wants to do. It enables him/her to bypass the traditional academic post-doctoral phase and have intellectual and funding independence. The hope is that GIS Fellows will develop and run research programmes that enhance the research portfolio of GIS and will propel them over the course of 3-6 years into full-fledged investigators.

GIS CLINICIAN SCIENTIST (CS) FELLOW

The GIS CS Fellow programme is aimed at supporting the development of the Clinician Scientist leaders of the future. The exposure to GIS' environment of cutting-edge technology and integrative science will enhance their training and the scientific impact and innovation/creativity of their research. The hope is that the GIS CS Fellows will strengthen the translational interface of GIS and through this programme develop into a successful independent Clinician Scientists.

GIS INNOVATION FELLOW

The GIS Innovation Fellow programme is geared for the accomplished PhD graduate who has demonstrated a capability to advance research ideas into a path for commercial development. The expectation is that the GIS Innovation Fellow will develop and implement a business plan to create a new start-up or spin-off company within three years.

Candidates for these programmes should show exceptional promise to develop into world class researchers and their work is expected to further strengthen the key strategic research areas of GIS. For further information on these programmes, visit the GIS website or email **FellowsRecruit@gis.a-star.edu.sg**.

GIS Clinician Scientist Fellows

GIS Innovation Fellows (Left to right)
Oliver **WORSLEY** / Astrid **IRWANTO** / Justin **TAN**

GIS Fellows (Left to right)
CHEN Kok Hao / Sho **GOH** / **CHEW** Wei Leong

GIS Clinician Scientist Fellows (Left to right)
Iain **TAN** / Daniel **TAN**

POST-DOCTORAL PROGRAMMES

GIS attracts highly-motivated postdoctoral researchers from Asia and around the world. Our well-equipped laboratories and collaborative culture offer ideal postdoctoral training for individuals engaged in cutting-edge research at the interface of molecular biology and biochemistry, genomic technology, and scientific computing. Our postdocs work in diverse fields, from cancer biology to stem cell genomics, infectious diseases to population genetics. Postdocs receive competitive salaries and are encouraged to attend international conferences to stay current in their fields of expertise.

Interested applicants should visit our website and apply directly to laboratories of interest.

GRADUATE PROGRAMMES

GIS welcomes PhD students who are eager to apply modern genomic technologies to problems that lie at the intersection of basic biology and its applications to medicine. The collaborative research environment at GIS is conducive to the training of modern biologists, who increasingly require access to technologies and expertise that lie beyond the realm of a single laboratory.

GIS and its parent organisation, A*STAR, are not universities and cannot offer PhD degrees directly. However, strong links have been established between GIS and graduate programmes within Singapore to provide PhD students the opportunity to engage in projects at GIS. Most of our PhD students are enrolled in the graduate programmes of either the National University of Singapore (NUS) or Nanyang Technological University (NTU). In addition, we have a number of international students working towards their PhD at GIS through partnership programmes between A*STAR and affiliated universities.

Different funding mechanisms are available for Singaporean and foreign students. For more information on PhD programmes, please refer to the A*STAR website (www.a-star.edu.sg) under the tab of Scholarships.

ATTACHMENT PROGRAMMES

GIS welcomes applications from university and polytechnic students for our research attachment programme. Students who do attachments at GIS have the opportunity to participate in exciting, modern biological research alongside our scientific staff. In order to have a meaningful research experience, we encourage an attachment duration of at least 12 weeks full-time (or the equivalent in a part-time attachment). Experience at GIS has led to several of our attachment students moving on to graduate programmes.

Deniz DEMIRCIOGLU, PhD student, Singapore International Graduate Award Scholarship
GIS provides a multi-cultural and multi-disciplinary working environment for everyone from any background. The interdisciplinary research approach allows me to expand my horizon and prepares me for future research problems.

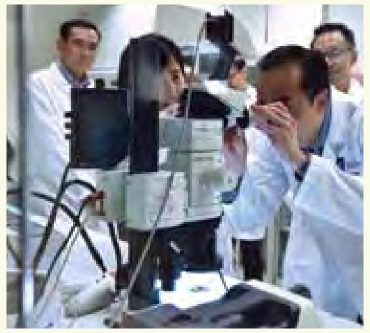
Sarah Catherine GEIGER, student attachment, Singapore International Graduate Award Scholarship
The unique environment at GIS challenges me to always think beyond the academic implications of my work, and the researchers here clearly want to make a difference in the world. Day by day, I know that I am growing as a student, a scientist, and as a person.

Oguz GOKCE, post-doctoral fellow
GIS gives me the opportunity to work with people from different backgrounds in a multi-disciplinary environment. Most importantly, it feels amazing to play a part in the projects that can be translated from lab to the clinic directly.

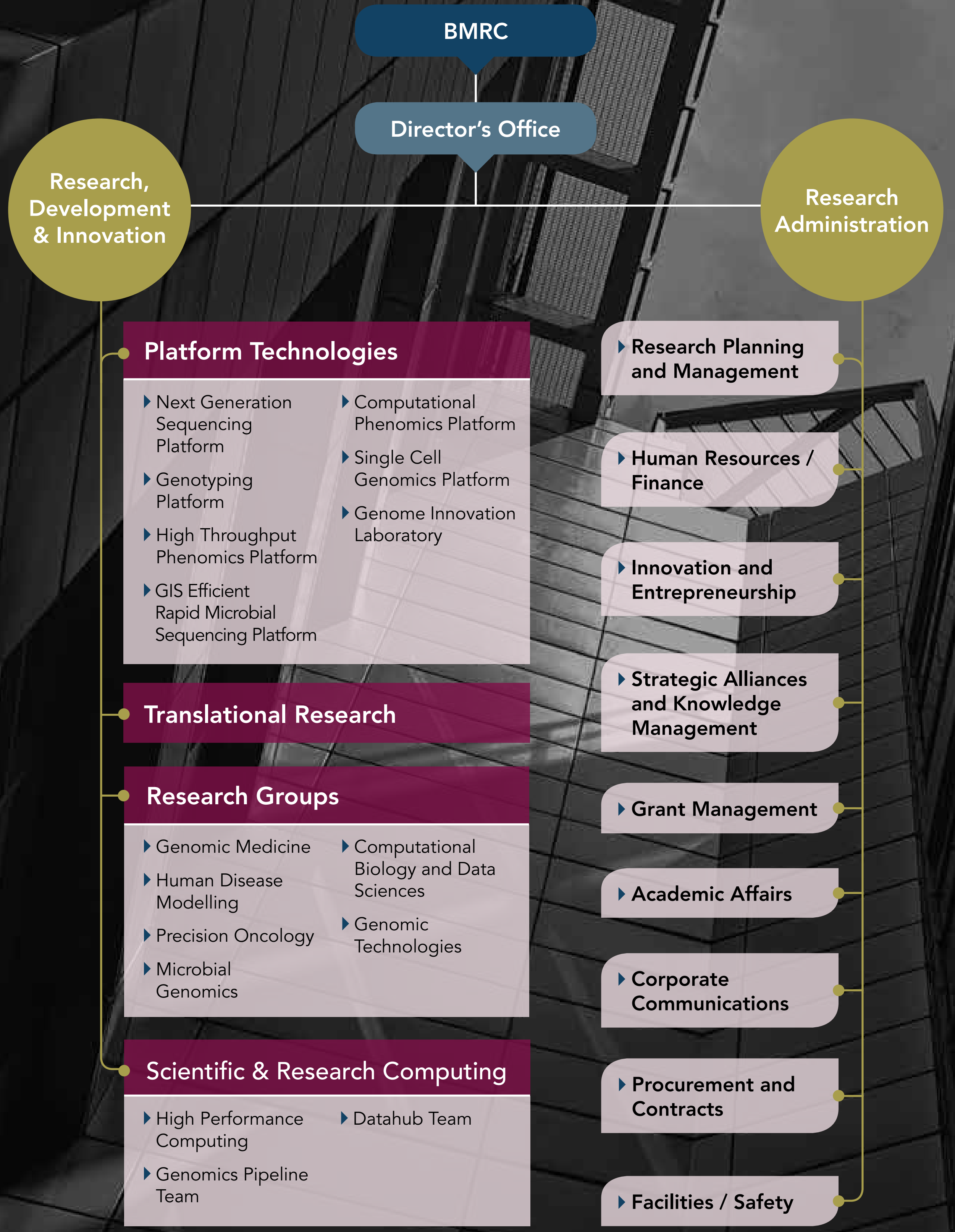
Jane LEE Jia Hui, PhD student, A*STAR Graduate Scholarship
From this twinkle-eyed dyslexic PhD student's perspective, GIS not only has an awesome community but there is always an exciting research hotpot brewing here. How not to love it? It is truly inspiring to see first-hand how quality science and our cancer therapeutic approaches are impacting lives.

OUR COMMUNITY

The Genome Institute of Singapore is well known for its positive atmosphere, and collaborative approach towards research. Our people are passionate about what they do and are the drivers behind GIS' success. We are constantly improving ourselves and pushing each other to be the best that we can be, be it at work or play. We strive to create platforms for great minds to share their knowledge and expertise. Here's a peek into the community and activities at GIS.



ORGANISATION CHART



- BMRC
  - Director's Office
    - Research, Development & Innovation
      - Platform Technologies
        - Next Generation Sequencing Platform
        - Genotyping Platform
        - High Throughput Phenomics Platform
        - GIS Efficient Rapid Microbial Sequencing Platform
        - Computational Phenomics Platform
        - Single Cell Genomics Platform
        - Genome Innovation Laboratory
      - Translational Research
      - Research Groups
        - Genomic Medicine
        - Human Disease Modelling
        - Precision Oncology
        - Microbial Genomics
        - Computational Biology and Data Sciences
        - Genomic Technologies
      - Scientific & Research Computing
        - High Performance Computing
        - Genomics Pipeline Team
        - Datahub Team
    - Research Administration
      - Research Planning and Management
      - Human Resources / Finance
      - Innovation and Entrepreneurship
      - Strategic Alliances and Knowledge Management
      - Grant Management
      - Academic Affairs
      - Corporate Communications
      - Procurement and Contracts
      - Facilities / Safety

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