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WELCOME MESSAGE FROM
PROFESSOR
NG HUCK HUI

Executive Director
Genome Institute of Singapore

The Genome Institute of Singapore is a unique place for scientific discovery. We believe that a future in biology lies in the fusion of highly comprehensive and massively parallel genomic and computational approaches with cell and medical biology. Therefore, we seek the integration of technology and biology towards answering questions of medical importance.

We will support this vision by creating a social culture that encourages open communication, fluid organisational structures and teamwork, but without diminishing individual effort.

Our approach is strategic and is based on long-term scientific and social objectives. I am very pleased to be leading this noble effort, excited about our future and delighted with the colleagues who have decided to join us on this adventure.
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.
BACKGROUND

In December 2011, Professor Ng Huck Hui took over the reins as GIS’ new Acting Executive Director. Prof Ng is one of Singapore’s most prominent scientists in stem cell research. He has won numerous prestigious awards including 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. Prof Ng was subsequently appointed GIS’ second Executive Director in October 2012.

The Agency for Science and Technology Research (A*STAR) is the parent funding body for the 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 meter 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, 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-art research infrastructure with entertainment and educational facilities.

In mid 2008, the engineering research institutes were relocated to newly-constructed facilities called Fusionopolis, also within the Buona Vista Science 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 focuses 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, the 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 modeling.

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, High-throughput Biology, Genome Engineering, Genotyping, Cytogenetics, Single Cell Genomics). We have a cohort of exceptional young scientists in our GIS fellows programme 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.
RECOGNITION

FUNDING
In benchmarking ourselves on the international stage, we have, since our inception, competed successfully for several millions of dollars of external funds each year in the form of research grants from the US National Institutes of Health (NCI, NHGRI, NIDDK), European Union, and the US Defense Department, and various private foundations. We have used these resources to build strong collaborative links with 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 companies such as GlaxoSmithKline, Roche, Eli Lilly and Novartis to develop treatments and diagnostics for diseases such as hepatitis, cancer and dengue fever.

NATIONAL CONTRIBUTIONS
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 Prof 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 Prof 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.”
Crisis Management Group

Based on our national service work during the SARS crisis, the GIS has been invited to participate in the crossministerial Crisis Management Group that plans the national response to pandemic threats.

The 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; in 2009, as in 2003, the 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 sprung 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, 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 the 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.
GIS-SPONSORED EVENTS

2013 BHC-NTU-GIS Joint Seminar
The British High Commission, Lee Kong Chian School of Medicine (Nanyang Technology University) and GIS jointly organised a seminar by Professor Sara M Rankin, Professor of Leukocyte and Stem Cell Biology, National Heart and Lung Institute, Imperial College London on 28 February 2013. Titled Regenerative Pharmacology - Developing New Therapies to Mobilise Stem Cells from the Bone Marrow, the seminar was another instalment of the “UK-Singapore Partners in Science” initiative.

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.

RNAi Asia 2011
Select Biosciences and GIS organised a second round of the RNAi Asia conference on 22 and 23 November 2011, chaired by Dr Lim Bing. It was organised in conjunction with Screening Asia and Molecular Diagnostics Asia.

ChIA-PET Analysis Workshop 2011: Methods for a Chromatin Interaction Analysis
Genomes are organised into high-order architectures for functions. However, little is known at molecular levels how chromosomes are organised and what types of structural platforms are implemented for genome functions. The ChIA-PET method was developed to address these questions. In this approach, long-range chromatin interactions are captured by formaldehyde cross-linking and the fragmented DNA-protein complexes are enriched by chromatin immunoprecipitation (ChIP). Tethered DNA fragments in each of the chromatin complexes are joined to each other via DNA linkers through proximity ligation. Paired-End diTags are extracted from the ligation products, and are analysed by massive parallel high-throughput sequencing. The ChIA-PET tag reads are then mapped to reference genome sequences to reveal contacting information between remote DNA elements presumably brought together in close spatial proximity by target protein factors.

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.

Personalized 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 were on cancer genetics, genetics mutation, gene expression regulation, disease-specific concerns, and targeted therapeutics. Chaired by Prof Edison Liu, the conference attracted a 300-strong participation across the globe.

RNAi Asia Conference 2010
In partnership with Select Biosciences, GIS hosted the 2nd annual RNAi Asia conference in Biopolis, Singapore. This event was chaired by Dr Lim Bing of the Genome Institute of Singapore with a focus on RNAi/microRNA research and business to serve the Asian market. Held on 15 and 16 November 2010, the conference was organised in conjunction with Screening Asia.
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 the GIS and the Finals of the competition was telecast in August over Channel 5. Prof 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.

Yeast and Fungal Biology 2009
The Yeast and Fungal Biology Symposium was held in April 2009. Especially catered to post-doctoral participants in preparation for scientific independence, it was organised by post-docs from the GIS and the Temasek Life Sciences Laboratory. Among the experts present were keynote speaker Dr. Alex Andrianopoulos, the Howard Hughes Medical Institute International Scholar, and a renowned geneticist specialised in the field of pathogenic fungi and host interaction at the University of Melbourne. Over 70 local and overseas post-docs and PhD students attended the symposium.

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 the 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, and 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 South East Asia.

Asia-Pacific Regional S.pombe Meeting 2008
Renowned research scientists from the US, Europe and Asia attended the Asia-Pacific Regional S.pombe Meeting from 25 – 27 July 2008 in Singapore. Organised by Dr Jianhua Liu of the GIS and Dr Mohan Balasubramanian of the Temasek Life Science Laboratory, it was the first international S.pombe meeting.

STUDENT PARTICIPANTS OF THE NATIONAL SCIENCE CHALLENGE 2010 GIVING A PRESENTATION HOSTED AT THE GIS
held in Singapore that focused on studies such as cell cycle regulation, DNA replication, mitosis and meiosis, cytokinesis and cell division, cytoskeleton, and chromatin structure, using the unicellular model organism S. pombe. President of the Rockefeller University and Nobel laureate Sir Paul Nurse, renowned scientists Dr Richard Losick of Harvard University, Dr Randy Schekman of UC Berkeley, Dr Masayuki Yamamoto of the University of Tokyo, and Dr Yue Wang of the Institute of Molecular and Cell Biology Singapore presented their keynote speeches during the meeting. This meeting attracted over 100 overseas and 80 local participants from more than 10 countries.

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 the 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 is 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 T. Liu of the 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 and 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.
L’Oréal-UNESCO for Women in Science International Fellowship 2014  
Dr Li Jingmei, Research Fellow, Human Genetics  
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. Her work aims to identify genetic factors that may give rise to aggressive tumours.

Young Scientist Award 2013  
Dr Khor Chiea Chuen, Senior Research Scientist, Human Genetics  
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.

The Outstanding Young Persons Singapore (TOYP) Award 2013  
Dr Khor Chiea Chuen, Senior Research Scientist, Infectious Diseases  
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, Infectious Diseases Group  
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  
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. A candidate must be a graduate student who is pursuing a degree of Doctor of Philosophy (PhD) in an institution located in mainland China, Hong Kong, Taiwan, or Singapore.

President’s Science Award 2011  
Drs Bing Lim, Lawrence Stanton, Ng Huck Hui and Paul Robson, Stem Cell and Developmental Biology  
were conferred the award by H.E. President Tony Tan for their groundbreaking work on the regulatory pathways controlling embryonic stem cell pluripotency and cell fate decisions.

Over the past nine years, the stem cell group at GIS has comprehensively assessed genes required for stem cell function, and helped to define the specific functions of these genes through cutting-edge genetic technologies, such as genome-wide sequencing. These efforts have led to the discovery and definition of novel regulatory factors required for the functions of embryonic stem (ES) and other stem cells.

The team’s work has advanced the capability to maintain and expand ES cells, and to direct their differentiation to create specialised cell types. This knowledge is critical for the successful application of stem cells for therapeutic, translational and academic purposes, particularly in providing industry, clinicians, or researchers with a variety of specific cell types needed for medical therapies, biotechnology applications and research experiments.
The Chen New Investigator Award 2011
Dr Jianjun Liu, Senior Group Leader, Human Genetics Group

Dr Liu was presented with the Chen New Investigator Award from the Human Genome Organization. This award is given to the top young scientists in Asia studying human genetics and genomics.

Singapore Youth Award 2010
Dr Jonathan Loh, Research Fellow and GIS Graduate Student, Stem Cell & Development Biology

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. Dr Huck Hui Ng won the same award in 2005.

The Medal of Commendation 2010
Dr Huck Hui Ng, Senior Group Leader, Stem Cell & Developmental Biology

Dr Ng was conferred the Medal of Commendation in 2010, for having inspired and mentored many young scientists, including Dr Jonathan Loh, who received the Singapore Young Scientist Award in 2009.

The Chen New Investigator Award 2010
Dr Huck Hui Ng, Senior Group Leader, Stem Cell & Developmental Biology

Dr Ng was presented with the Chen New Investigator Award in 2010. This award is given 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 Nguyen Minh, Post-Doctoral Fellow, Stem Cell & Developmental Biology, and Melissa Jane Fullwood, Post-Doctoral Fellow, Genome Technology & Biology

GIS scientists Dr Le Thi Nguyen Minh and Dr Melissa 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

Prof 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 Huck Hui Ng, Senior Group Leader, Stem Cell & Developmental Biology

Dr Ng was one of the recipients for the TOYP Awards in 2009. The TOYP Awards 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

Prof Edison 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**

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

National Science Award 2007  
**Dr Huck Hui Ng, Senior Group Leader, Stem Cell & Developmental Biology**

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.

National Science Award 2006  
**Senior Group Leaders Drs Yijun Ruan, Ken Sung, Chia Lin Wei and Patrick Ng**

were awarded the National Science Award 2006 for their innovative work in developing the Paired End diTag technology for comprehensive characterisation of the human genome and transcriptomes.

Based on the Paired End diTags (PET) strategy, the team devised Gene Identification Signature (GIS) analysis to precisely demarcate the boundaries of gene coding regions and invented the ChiP-PET (chromatin immuno-precipitation coupled with paired-end ditagging) analysis for highly accurate, robust and unbiased genome-wide identification of transcription factor binding sites in the genome. With the newly developed multiplex sequencing (MS-PET) method, the PET sequencing strategy can achieve over 100-fold efficiency improvement. The team also developed total computational solutions to accommodate and process the high volume of data generated. Collectively, they established an integrated, high throughput and high precision technology platform for the comprehensive characterisation of the human genome and transcriptome.

The team has numerous publications on their invention and exciting biological discoveries in prestigious journals. They were also awarded a USD $1-million grant by NIH to further develop their technology.

NUS Centennial Genesis Award 2005  
**Dr Bernard Leong, Research Scientist, Information and Mathematical Sciences**

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. The company has produced a kit that will predict liver heptotoxicity cheaply, accurately and efficiently.

Great Women of Our Time 2005  
**“Most Inspiring Woman”**  
**Dr Lisa Ng, Research Scientist, Cell and Medical Biology**

GIS scientist Dr Lisa 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. The annual gala event recognises the outstanding accomplishments of women from the arts, finance, public service, science, sports and design.

Young Scientist Award 2004  
**Dr Huck Hui Ng, Group Leader, Stem Cell & Developmental Biology**

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. Dr Ng studies the regulation of gene expression at different levels: epigenetic, chromatin-mediated, and transcription factor-driven. He had previously uncovered novel links between transcription, chromatin and epigenetic modifications. These works are of fundamental significance, and have been highly cited.
RESEARCH PARTNERS

EMPOWERING RESEARCH

We are at the onset of a revolution in genomics-based health and life sciences. Advances in genomic technologies, genetic engineering, computational biology, disease model systems, and molecular cell biology are generating discoveries with remarkable speed that are leading us to novel and precise therapies for human diseases. Therapies from population studies designed for the impersonal average patient are going to be replaced by individualised care, tailored to the individual’s genetic and biochemical makeup – a new paradigm in personalised medicine.

To make this promise a reality, we must advance from a focus on single gene effects to understanding and controlling the complex interactions throughout the networks of all genes involved in health and disease contexts. New innovations in the genomics space put mastery of biological complexity within our reach. With creative use of such new technologies and tools, we can devise definitive solutions to complex medical problems and develop a truly translational biomedical approach.

At the Genome Institute of Singapore we believe in providing an environment where innovation can flourish.

collaboratively with our partners. Recognised as a leader in genomic research to partner with, we have a strong desire to deliver future success for our partners and for our institute.

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, research and development, translational biosciences like stratified oncology and (companion) diagnostics.

The focus of each of our alliances is on how we can create a sustainable win-win situation for all partners involved; our partners play an active role in the scientific and commercial development – we consider a variety of deal types that range from Research Collaboration Agreements (RCA), Project or Service Agreements (PA), Licensing (LA), Joint Labs and Centres of Excellence (CoE).

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

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

In the setup of a Joint Lab or Centre of Excellence, GIS engages with partners on a long-term strategic basis. Dedicated GIS resources become accessible to our partners and vice versa to advance research, technology transfer and capability building for our partners.

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 assists with identifying lines of communication and in establishing a governance structure.

ALLIANCES WITH INDUSTRY

Industrial Partnerships

Making an impact on the world around us is an important focus at the GIS. Through research collaborations with the industry, we seek to understand and solve complex application related questions in the genomics area.

The GIS is open to requests from the industry and our business development team works to facilitate project management and coordination with our research groups. Successful collaborations with many of the world’s leading pharmaceutical, diagnostic and biotech companies have been carried out at the GIS, to the extent that we have built a strong repute in the biotech and pharma environment. Studies have, for instance, covered areas like application developments, genomic studies, molecular diagnostic development, visualisation of complex genomics data, and biomarker discovery or evaluations.

Together with one of the top 10 pharmaceutical companies, researchers at the GIS studied the
mechanisms of drug resistance in tuberculosis. This project involved gene expression microarray and RNA sequencing and resulted in valuable data for the company’s drug development efforts.

The Computational and Systems Biology department deals with research around datasets with strong focus on finding cutting edge solutions for data processing and alignment algorithms. In a recent collaboration, novel cloud-based storage solutions for complex NGS data were developed.

Using our certified molecular diagnostics laboratories and expertise in assay development and validation, a recent product prototype was developed to stratify patients with Chronic Myelogenous Leukemia (CML) for the best available treatment.

In addition to the more strategic research collaborations, the teams at the GIS also offer consultancy and expert advice in the research focus areas as well as service-based agreements covering sequencing, real time PCR and molecular or companion diagnostics development.

Besides the strong relations GIS has built with the biomedical industry, we establish a strong network with our clinical and academic partners to enhance knowledge exchange, bench-to-bedside translation and to make an impact on medical healthcare through genomics, worldwide.

**SELECTED ALLIANCES WITH OUR CLINICAL PARTNERS**
- Alexandra Hospital (Singapore)
- Cancer Science Institute (Singapore)
- Duke-NUS Graduate Medical School (Singapore)
- Khoo Teck Puat Hospital (Singapore)
- KK Women’s and Children’s Hospital (Singapore)
- Lee Kong Chian School of Medicine, NTU (Singapore)
- National Cancer Centre (Singapore)
- National Neuroscience Institute (Singapore)
- National University Health System (Singapore)
- National University Hospital (Singapore)
- Singapore General Hospital (Singapore)
- Singapore National Eye Center (Singapore)
- Tan Tock Seng Hospital (Singapore)
- Amsterdam Medical Center (Holland)
- Eye & ENT Hospital Fudan University (China)
- Hospital Clínico Universitario de Santiago de Compostela (Spain)
- John Wayne Cancer Institute (CA, US)
- Sichuan academy of Medical Sciences and Sichuan Provincial People’s Hospital (China)

**SELECTED ALLIANCES WITH OUR ACADEMIC PARTNERS**
- Nanyang Technological University (Singapore)
- National University of Singapore (Singapore)
- Center for Cellular and Molecular Biology, Hyderabad (India)
- Hadassah-Hebrew University (Israel)
- Imperial College London (UK)
- Indian Statistical Institute (India)
- Karolinska Institute (Sweden)
- Medical Research Council (UK)
- Queen Mary University of London (UK)
- Seoul National University (Korea)
- Shandong Provincial Institute of Dermatology and Venereology (China)
- The University of California, San Diego (US)
- University of Bonn (Germany)
- University of Sydney (Australia)
- University of California, Los Angeles (US)

GIS strives to build a framework for strategic alliances, entrepreneurship and translating research outputs for public’s health together with industry, academia, clinicians and policy stakeholders, and we like to be the preferred partner for research and practice of biomedical innovation.

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

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.

At the GIS, we have seven areas of research focus that are run by our teams of outstanding scientists:

- Human Genetics
- Infectious Diseases
- Cancer Therapeutics and Stratified Oncology
- Stem Cell and Regenerative Biology
- Cancer Stem Cell Biology
- Computational and Systems Biology
- Translational Research
HUMAN GENETICS

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

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 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, pseudoxfoliation syndrome, and extreme myopia) and optic traits (central corneal thickness, optic nerve head 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.

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 the 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 pluripotent 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.

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.

Our research is highly collaborative through extensive cooperation with local and international clinical research groups and hospitals, close integration with genomic technologies and computational biology, and multi-discipline efforts with other research domains on investigating functional impact.
INFECTIONOUS DISEASES

GIS has utilised cutting edge genomic technology platforms to investigate infectious diseases from multiple perspectives. By looking at the genomes of both the pathogen and the host, together with their transcriptomic responses, we have enabled a rapid understanding of the host pathogen interaction during infectious diseases.

We aim to decipher the specific effects of variation in the genomes of the host and the pathogen using global networks, both in vivo and in vitro. Our technological capabilities are being applied to patient samples, at large scales, for diagnosis and patient characterisation. These approaches allow us to perform molecular epidemiological studies on a range of disease, from Dengue, Tuberculosis, Urinary tract infections to SARS, avian influenza and a full range of others. Increasingly, this is also allowing us to evaluate the evolution of natural pathogen
isolates, using population diversity to investigate the causes of disease and disease severity. 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 emerging infectious threats to human health.

The raw genetic data is handled by the Computational and Systems Biology group, who is developing novel analytical approaches for data organisation and analyses that are critical to further deciphering the evolution and epidemiology of infectious diseases. These tools are being utilised across the community to ensure impact.

We also investigate human health, from understanding the genetic basis of a successful vaccine response, to understanding healthy skin and gut biomes. With probiotic dairy products developing into one of the most successful categories of functional foods, we are also investigating how these biomes may be enhanced, with wide applications to other, perhaps unexpected, conditions such as inflammatory and autoimmune diseases and cancer development.

THE GIS EFFICIENT RAPID MICROBIAL SEQUENCING (GERMS) PROGRAMME

Our pathogen sequencing infrastructure (termed the GERMS platform) is dedicated to microbial sequencing, including viruses, bacteria and fungi, with both DNA and RNA (including transcriptome) analyses. We are also targeting microbial communities (biomes and metagenomics) and have a wide range of sample types under investigation (from skin, eye, throat, gut, etc.) from humans, environments and animals. Microbes often have distinct challenges compared to human sequencing and GERMS leverages ongoing improvements in sequencing (including new technologies such as Pac Bio) to be specifically designed for microbial efficiency, scalability, and reliability.

The GERMS programme has many active collaborations with intra-institute, national and international collaborators from industry to academic backgrounds alike. The team is able to offer a complete package, from project design to sample handling, sequencing strategies, cutting edge analysis pipelines and comprehensive interpretation. Recent work includes clinical trial analysis of the effect of therapeutics on dengue viruses with Roche, microbiome high throughput approaches using Illumina, tuberculosis drug screening techniques using bacterial RNA with Novartis and whole genome sequencing of streptococcal pneumonia isolates from every hospital in Singapore.
CANCER THERAPEUTICS AND STRATIFIED ONCOLOGY

Cancer represents a complex disease state where cellular interactions at multiple levels, including genetic, epigenetic, and transcriptomic, combine to establish a robust adaptive system that maintains cancer cell survival, even in the face of therapeutic interventions. Understanding the fundamental governing principles of this immense complexity is critical for developing novel and more effective treatments to inhibit cancer aggressiveness, metastasis and drug resistance.

The Cancer Therapeutics and Stratified Oncology group at the GIS uses a variety of advanced and
contemporary technology platforms to generate and analyse high-quality multi-dimensional data sets associated with cancer, to answer fundamental questions concerning tumour cell death and survival.

Our research programmes integrate functional genomics, chemical biology, deep sequencing, and computational biology, interpreted through a systems biology perspective, to identify key elements critical to maintaining the biological phenotypes of cancer cells. Key areas of strength involve the identification of synthetic lethal gene-gene interactions, genomic alterations related to patient clinical outcome, and the development of novel strategies for cancer therapy.

Our team is also striving to translate our basic discoveries into applications for clinical impact. To this end, we have initiated POLARIS (Personalized OMIC Lattice for Advanced Research and Improving Stratification), a strategic initiative for introducing and embedding genomic information into the diagnosis and treatment of medical diseases in Singapore. Formed as a partnership between multiple A*STAR Research Institute and public healthcare centres, the POLARIS consortium will establish clinically certified genomic and metabolomic platforms, develop technologies for processing clinical samples, and develop informatic pipelines for results analysis, data interpretation, and clinician reporting. Through this effort, we seek to establish a unified national framework for the pursuit of “Clinical OMICS”.

Senior Investigators
Patrick TAN / YU Qiang
Ramanuj DASGUPTA / Axel HILLMER
LIM Bing
Frank MCKEON
STEM CELL AND REGENERATIVE BIOLOGY

The application of genomics technologies to explore stem cell biology has been a pillar of research at the GIS since its inception. Stem cells have the unique and defining characteristics of unlimited self-renewal and the capacity to differentiate into progeny cells of specialised functions. This has spawned heightened interest in using stem cells for a variety of applications in the field of regenerative medicine. By combining expertise in cell biology, developmental biology, genomics technologies and bioinformatics, we have established a remarkable track record in dissecting the regulatory networks that control stem cell function. Our work has led to fundamental discoveries in how cell fates are specified during normal
development and provided key insights into the molecular basis of cellular reprogramming.

Having gained a firm understanding of how cell fates are controlled, the programme is now capitalising upon this knowledge. Directed differentiation of stem cells now allows us to generate human cells and multicellular tissues in a culture dish. For example, the teams are now growing human neurons, liver cells, and heart cells from both healthy individuals as well as patients who are afflicted with debilitating genetic diseases. This line of research is yielding a trove of information about the molecular basis of many diseases, which we are translating into novel diagnostics and therapeutics through partnerships with clinicians and pharmaceutical companies. The programme is also taking advantage of new genome editing technologies to introduce and repair genetic variations in stem cells and their differentiated progeny to study the function of these genes in biology and disease.
CANCER STEM CELL BIOLOGY

Malignant tumours are highly heterogeneous, consisting of cancer cells intermingled with blood vessels and stromal cells. The cancer cell population itself is also a constellation of different cell types contributing to the unique histopathological features of specific cancers.

There is now substantial evidence that only a subpopulation of ‘tumour initiating cells’ are capable of proliferating, differentiating and maintaining tumour growth and phenotype. Tumour Initiating Cells (TICs), or Cancer Stem Cells (CSCs), first identified and characterised in leukemias, have been described in several solid tumours, including breast, colon, brain and prostate. Most recently, we have described the isolation of TICs for lung adenocarcinoma. It is most likely that with careful experimental designs, TICs can be identified and isolated from all human cancers.
This has opened up new avenues to explore in our war against cancer. Our recent work with lung cancer TICs has, for example, revealed new and exciting therapeutic pathways and targets.

The GIS cancer stem cell programme is built around a series of logical progressive steps:

1. To develop methods to identify and isolate TICs from many different solid cancers (e.g. liver, pancreas, stomach). We have established both in vitro and in vivo methods to clone TICs and establish tumour cell lines. New cell culture methods are being developed to study and understand the heterogeneity and relationship between cancer and non-cancer subpopulations of tumours.

2. To fully characterise, at the cellular and molecular level, TICs from different tumours. We make full use of the wide repertoire of genomic tools and technology available in the GIS to characterise TICs including RNAseq, whole exome sequencing, histone markings and methylation patterns and structural variation. These studies are carried out in either pooled populations, or where informative, at the single cell level.

3. To develop new strategies to eliminate each type of TICs, including identifying the most promising therapeutic targets. A major effort is to identify, from deep analysis of TICs, new therapeutic pathways such as the new Serine Glycine pathway we have recently discovered in lung cancer TICs. Our goal is to quickly narrow down to good druggable targets, and develop assays to carry out high throughput drug screens.

4. To rapidly evolve TIC-specific treatment modalities into clinical trials. Hit compounds are taken through validation, in vivo toxicity and efficacy studies and channel through the most strategic route to lead to clinical trials.

5. To test the power of combining anti-TICs treatment with other treatment modalities.

Our ultimate goal is to discover new drugs that could, in combination with other drugs, eliminate TICs/CSCs in cancer.

Our expectations are that research into the biology of TICs/CSCs will have a significant impact on improving the control and elimination of many cancers.
Computational Biology is at the heart of genomics where we seek to integrate and analyse large and complex data sets in order to derive a more complete systems understanding of biological processes and diseases. This is driven by the development and application of sophisticated 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 (TFBS) profiling, metagenomics and single-cell omics. Our scientists bring to bear 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
A unique aspect of the algorithm development efforts in the GIS is the focus on bioinformatics tools with performance and optimality guarantees.

on genomic technologies, cancer, stem cells and development, human genetics and infectious diseases.

The development of novel algorithms at the GIS is defined by two key strengths:

1. **Optimal algorithms with performance guarantees.**

2. **Algorithms for nextgen technologies.** CSB researchers have extensive experience designing methods to analyse novel datasets from cutting-edge genomic technologies and assays such as ChIA-PET, RNA Structure Probing, Single-cell Omics and Optical Mapping. These have allowed scientists at the GIS and researchers around the world to explore uncharted territories in genomic biology.

The computational tools developed at the GIS are designed for and brought to bear on a diverse array of questions in evolutionary and genomic biology including the following central themes in the CSB programme:

- Can we predict the impact of mutations (substitutions and indels) on protein function?
- How do we improve diagnostics for common and rare disorders from genomic information?
- What is the role of non-coding sequences in the human genome and how can we identify and characterise disease-causing non-coding polymorphisms?
- What is the molecular basis of human-specific traits and how did they evolve?
- Can patient-specific driver mutations be predicted and used to personalise cancer therapy?
- How do viruses evolve and evade the immune system and can we effectively reconstruct their transmission patterns?
- What is the role of microbial communities in the human body in health and disease states?
Translational Research

With just over a decade of history, the Genome Institute of Singapore already enjoys international recognition as a quality organisation with a global vision that seeks to use genomic sciences to improve public health and public prosperity. The GIS continues to accumulate new discoveries in genomics, and publish high-level research papers in top scientific journals. In recent years, we have expanded our focus to include direct industrial applications for these findings. The critical challenge facing academic centres like our institute is translating basic research and new technology towards clinical utility.
Our main focus is on molecular diagnostics, which plays a central role in translational research.

The Translational Research group promotes the smooth transition from basic research to advances in science and technology, and hence to innovation. Our main focus is on molecular diagnostics, which plays a central role in translational research.

We are able to develop diagnostics for all assay formats and disease areas. Translational research can provide strong evidence that newly discovered biomarkers can be a significant tool for personalised patient care. Our support to the various GIS research groups by assay development, optimisation and validation significantly shortens the distance to commercial applications.

Leveraging on GIS’ experience in collaborative interdisciplinary research activities, the Translational Research group facilitates interactions between investigators from different fields such as biotechnology companies, pharmacology companies and hospitals.

The GIS is equipped with the most advanced technology platforms necessary for research and development in genomics, and application of genomic techniques to biological and medical questions. These technologies, such as the Next Generation Sequencing platforms, are accessible to members of the research community. Additionally, in order to adhere to industrial standards, our newly designed and constructed molecular diagnostics lab follows regulatory obligations and compliances.
PLATFORM TECHNOLOGIES
NEXT GENERATION SEQUENCING PLATFORM

Established 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 35 TeraBytes or 40 Gigabases per year. These include 200 million reads of up to 250bp per flowcell, in as short as a two-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 is also moving towards automating the process with a Biomek FX liquid handler, which will further increase its throughput and efficiency. We aspire to provide high quality sequencing support for the research community in Singapore and beyond.

GENOTYPING PLATFORM

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 the 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 the GIS multidisciplinary research teams in human genetics, cancer biology and stratified oncology, stem cells, and with researchers across America, Asia and Europe.

HIGH THROUGHPUT CELLULAR BIOLOGY PLATFORM

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 will ultimately enable the practice of targeted treatments, a first step towards personalised medicine.
The mission of the GIS High Throughput Cellular Biology (GIS-HTCB) Platform is to enable the discovery of new gene functions and phenotypes after specific gene depletion or over-expression, and identification of new chemical or biological entities that induce equivalent phenotypes. In addition, we are also interested to build predictive toxicity screening using relevant 3D/ Organotypic cell culture models.

The GIS-HTCB Platform specialises in functional genomics as well as target validation and small molecule optimisation through screening. A team with industrial and academic experience is available to aid investigators in their assay optimisation and screening activities. Laboratory automation provides RNAi screening easily applicable to most cell types, allowing for the rapid interrogation of gene function of the entire genomes of human and mouse. The small molecule chemical compounds will be used for validation of potential new therapeutic targets being discovered in basic research. The combination of RNA interference and high throughput screening has opened a new frontier in the unbiased discovery of genes essential for specific biological processes or disease states. Utilising synthetic small RNA duplexes (siRNA) or small RNA hairpins (shRNA), specific genes are inactivated within cells. This “loss of function” assay aids in pinpointing the role of specific gene products in relevant cellular processes.

siRNAs/shRNAs targeting the human and mouse genome from Ambion and SIGMA companies are available at the GIS-HTCB Platform. Screens are routinely performed in 384 well format in triplicate. The platform also provides cDNA (ORF) libraries from Thermo to enable researchers with specific enhancer screen models. In addition, we also provide scientists with unique collections of chemical libraries to enable proof of principle and target validation studies.

The GIS-HTCB Platform houses cutting-edge liquid handling robots, including the Perkin Elmer Janus, Sciclone ALH3000, Beckman FX (96- and 384-well pipetting), Agilent BenchCel Barcode labeler, automated Bio-Tek plate washers, CO2 incubators, plate storage, Multiflow reagent dispenser and Tecan M1000 multi-mode reader with dual injector and stacker. The platform also houses a cutting-edge High Content image-based system for next-generation cell/chemical biology research and analysis in fixed or in live cells and cellular systems.

**GENOME ENGINEERING PLATFORM ● ●**

Rapid advances in ultra high throughput sequencing technologies have enabled the complete assembly of whole genomes from multiple organisms, including human. As a result, the catalogue of protein-coding and non-coding genes, cis-regulatory elements, and genetic variants has grown tremendously and will continue to expand as more genomes are sequenced. With the large amount of data available today, scientists, engineers, and doctors now face two major challenges. First, the functions of most genes and genetic variants are unknown. The regulatory networks controlling many important biological processes are also missing key components. Second, there is a critical need to develop and implement effective tools to modify
any genome for a myriad of medical and industrial applications.

The genome engineering platform (GEP) at the Genome Institute of Singapore is part of a larger cross-organisational research effort on synthetic biology and has the capabilities to responsibly modify the human and mouse genomes for different research purposes. Our work encompasses the generation of genetically altered mice, such as knockouts and knockins, tetraploid complementation assays, teratoma assays, generation and characterisation of induced pluripotent stem cells (iPSCs), and genome editing. We leverage on transcription activator-like effector nucleases (TALENs) and the CRISPR-Cas system to delete genes and to make precise changes to the genome, so as to gain functional insights into different classes of genes. We collaborate closely with research groups within GIS, other institutes in Singapore especially the universities, and overseas research laboratories.

SINGLE CELL GENOMICS PLATFORM

The GIS-Fluidigm 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 Centre is a collaboration between the Genome Institute of Singapore and Fluidigm Corporation, an industry leader in single-cell genomics.

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 between 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 the single-cell genomics technologies that are at the core of Fluidigm’s business so that scientists and clinicians within the Singapore research community remain on the cutting edge of scientific research.

The Centre 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 the GIS.

The GIS-Fluidigm Single Cell Omics Centre stands as a prime example of a mutually beneficial academic-industry partnership model that fully exploits the capabilities of the institute in biology, technology, and computational biology.

**CYTOGENETICS PLATFORM**

Over the last five years we have established and expanded the expertise provided by the cytogentic platform. Our unit can provide a myriad of services focusing on the study of chromosomes abnormalities. This knowledge could be applied not only to human cells but also to other model organisms, such as mouse, rat and pig cells. Our services are currently required by a large number of researchers from local institutions (research institutes, universities and hospitals).

We routinely perform karyotyping and G-banding experiments to detect gross abnormalities. We also have the capabilities to carry out spectral karyotyping (SKY). SKY analysis is a multi-fluorescence in situ hybridisation (FISH) method, which allows for a complete analysis of structural rearrangements by using a specific colour probe per chromosome. This approach is particularly indicated in complex cancer cell line analysis in mouse or human.

Our team of experts can design specific probes to detect the regions of interest and perform probe validation to ensure that the relevant area is efficiently tagged. We can perform home-made FISH on BAC clones, cosmids, PCR products and plasmids. Again, this could be done in human and mouse. To facilitate detection of unbalanced rearrangements (deletions and duplications), we offer Array Comparative Genomic Hybridisation (aCGH), available for human cell lines and tumour samples.

The portfolio of available cytogenetic analyses is constantly expanding.
CORPORATE SERVICES

The Corporate Services (CS) division of the GIS is the institute’s supporting arm. Not unlike the oil that lubricates the engine, the main function of the CS division is to ensure the smooth-running of the scientific research activities of the institute.

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

The GIS Corporate Services comprises the following offices:
- Administrative Management
- Corporate Communications
- Facilities and Maintenance
- Finance
- Human Resources
- Procurement and Contracts
- Research Administration
- Strategic Alliances and Knowledge Management
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 multidisciplinary environment at the 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.
GIS 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. Human Genomics
2. Cancer Genomics
3. Infectious Diseases
4. Genomics Technologies (sequencing, diagnostics and computational technologies)
5. Cancer Stem Cell Biology
6. Tissue Regeneration
7. Computational Biology

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.

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 the GIS. For further information on these programmes, visit the GIS website or email FellowsRecruit@gis.a-star.edu.sg.
POST-DOCTORAL PROGRAMMES

The GIS attracts highly-motivated post-doctoral researchers from Asia and around the world. Our well-equipped laboratories and collaborative culture offer ideal post-doctoral training for individuals engaged in cutting-edge research at the interface of molecular biology and biochemistry, genomic technology, and scientific computing. Our post-docs work in diverse fields, from cancer biology to stem cell genomics, infectious diseases to population genetics. Post-docs 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

The 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.

The GIS and its parent organisation, A*STAR, are not universities and cannot offer PhD degrees directly. However, strong links have been established between the GIS and graduate programmes within Singapore to provide PhD students the opportunity to engage in projects at the 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 the 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 Awards & Scholarships.

ATTACHMENT PROGRAMMES

The 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 the GIS has led to several of our attachment students moving on into graduate programmes.