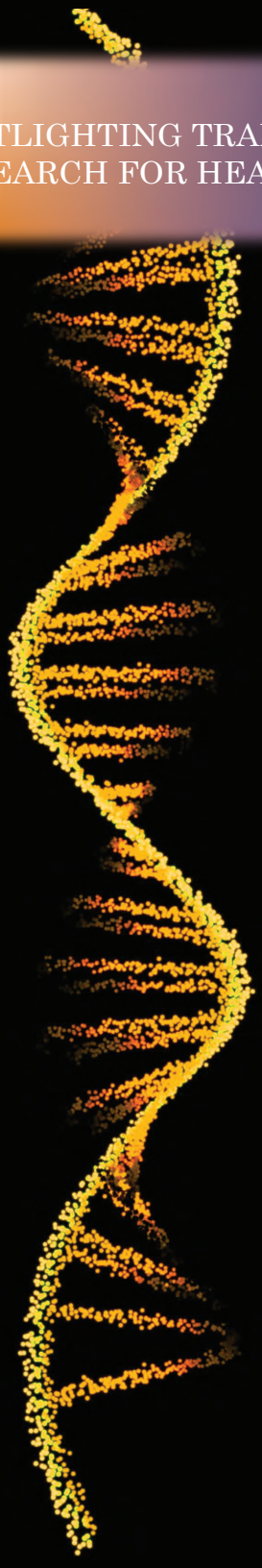
SPOTLIGHTING TRANSLATIONAL
RESEARCH FOR HEALTHCARE



NUS ncRNA Symposium & Liquid Biopsy Summit 2022

20th - 22nd September

National University Hospital
Auditorium, Singapore

NUS National University of Singapore | Precision Medicine Translational Research Programme, Yong Loo Lin School of Medicine

NUS National University of Singapore | NUS Centre for Cancer Research, Yong Loo Lin School of Medicine

NUHS National University Health System

mirxes TO KNOW. TO ACT.

CONTENTS

Welcome Message from the Organizing Committee

Distinguished guests and colleagues,

It is our immense pleasure to welcome you to the 2022 NUS non-coding RNA (ncRNA) Symposium and Liquid Biopsy Summit, co-organised by the Precision Medicine Translational Research Programme, NUS Centre for Cancer Research (N2CR), NUSMed ncRNA Core Facility and MiRXES Pte Ltd.

Identification of disease-specific molecular landscapes for proper patient stratification is pivotal to the success of precision medicine and precision health. Until recent years, RNA was known only as the key messenger between DNA and protein, the well-known central dogma in molecular biology. Today, we now know that the human genome encodes a vast repertoire of non-coding RNAs (ncRNAs). Furthermore, while these molecules were once dismissed as mysterious "dark matter", we can now see glimpses of how ncRNAs elegantly choreograph the intricate interplay between DNA, protein, and cellular function. The vast landscape of ncRNAs, which constitute more than 90 percent of RNAs made from the human genome, where most of the known ncRNAs have been discovered in the past 10 years and are largely unexplored.

This first-of-its kind translational research symposium brings together internationally renowned experts and many outstanding local researchers to share and discuss the latest development in ncRNA-based diagnostics, molecular functions and therapeutics. This year, we have included special sessions to discuss how Liquid Biopsy and Emerging Technologies can enhance the clinical management of patients. The NUS ncRNA Symposium aims to provide a vital platform for local and international researchers/clinicians to network and collaborate to collectively accelerate the clinical utility of ncRNA-based diagnostics and medicine to improve health and save lives in Singapore and worldwide.

We wish all participants an enjoyable and fruitful day of continuous learning and exchange of ideas in this symposium.

Best regards,

Prof Jimmy So. Dr Yvonne Tay, Dr Cheong Jit Kong and Dr Zhou Lihan
2022 NUS ncRNA Symposium Organising Committee

Dr Cheong Jit Kong

Precision Medicine TRP, NUS

Co-chair

Dr Yvonne Tay

N2CR, NUS

Prof Jimmy So

N2CR, NUS

Member

Dr Zhou Lihan

MiRXES Pte Ltd

The Symposium Organizers

Precision Medicine Translational Research Program

Precision medicine is an innovative approach that combines molecular data at system scale level (e.g. omics of genes, proteins, lipids, sugars, etc.) with environmental, lifestyle, and healthcare data to support research of molecular mechanisms, to optimize health and improve disease management of individuals. Large studies have successfully identified hundreds of novel loci associated with numerous diseases providing "map" of the locations in the genomes relevant to various disease states and clinical contexts.

The precision medicine translational research programme aims to identify therapeutic targets that can be modulated by novel strategies to treat or prevent disease. This approach is based on the belief that human genetics has the potential to accelerate the healing process through the modulation of the specific target even before any treatment begins.

NUS Centre for Cancer Research (N2CR)

Cancer is a leading cause of death and illness worldwide, and represents a present and growing challenge in Singapore. As such, the NUS Centre for Cancer Research (N2CR), one of ten new Translational Research Programmes (TRPs) in the National University of Singapore's Yong Loo Lin School of Medicine, aims to develop innovative new ways to detect, cure and prevent cancer by undertaking internationally leading fundamental research that advances the understanding of cancer, and by translating these research discoveries into clinical practice to benefit patients. N2CR's research aspires to further understand key genetic and epigenetic changes that drive the origin and progression of cancer in different tissues, particularly those forms prevalent in Asia; develop new therapies to target specific cancers in specific patients; and gain insights into the genetic and environmental variations that underlie cancer susceptibility.

N2CR is carefully organized to motivate interdisciplinary collaborations – spanning from bench to bedside and back again – to drive research in key areas. The N2CR empowers fundamental and clinical researchers from NUS Medicine, our core partners: the Cancer Science Institute of Singapore, and the National Cancer Institute of Singapore (NCIS) in the National University Health System (NUHS), to work together, alongside scientists and technologists from other disciplines, to address major scientific and clinical challenges. N2CR's work is enabled by cancer site-specific resources which include the collection of patient samples and databases with clinical information. It will focus on three cross-cutting themes that promote powerful interdisciplinary collaborations between fundamental researchers, enabling technologists and clinical investigators.

Scientific Programme
20 September 2022, Tuesday

Morning Session

7.30am **Registration**

Opening Address

8.30am **Chng Wee Joo**

Vice-Dean (Research), NUS Yong Loo Lin School of Medicine, Singapore
Provost's Chair Professor, NUS Department of Medicine, Singapore

8.45am **Yeoh Khay Guan**

Chief Executive, National University Health System, Singapore
Professor, Department of Medicine, NUS Yong Loo Lin School of Medicine, Singapore

Theme: Preventive and Precision Health – ncRNA Biomarkers (I)
Chair: A/Prof Too Heng-Phon
NUS Medicine, Singapore

9.00am **Tatsuro Murano**

Associate Professor, Department of Gastroenterology and Endoscopy, National Cancer Center Hospital East (NCCHE), Japan

Diagnostic performance of GASTROClear for detecting gastric cancer in the Japanese population

9.30am **Jan Heng**

Assistant Professor, Department of Pathology, BIDMC, Harvard Medical School, USA

Plasma miRNAs associated with cisplatin sensitivity in breast cancer

10.00am **Morning Tea Break**

10.20am **Frank Slack**

Director, Harvard Medical School Initiative for RNA Medicine, Beth Israel Deaconess Medical Center (BIDMC), United States
Shields Warren Mallinckrodt Professor, Department of Pathology, Harvard Medical School, USA

Keynote Lecture: *Towards microRNA-based cancer medicine*

11.30am **Lunch**

Scientific Programme
20 September 2022, Tuesday

Afternoon Session

Theme: ncRNA – Forms & Functions
Chair: Prof Frank Slack
Harvard Medical School, USA

12.30pm — **Polly Chen**

Associate Professor, Department of Anatomy, NUS Medicine, Singapore
Principal Investigator, Cancer Science Institute, Singapore

Noncoding natural antisense transcripts (ncNAT) Influence Promoter Usage of Their Counterpart Sense Genes in Cancer

1.00pm — **Yvonne Tay**

President Assistant Professor, Department of Biochemistry, NUS
Principal Investigator, Cancer Science Institute of Singapore, NUS

Widespread 3'UTR splicing promotes oncogene expression and tumorigenesis

1.30pm — **Giovanni Blandino**

Director, Translational Oncology Research Unit, Regina Elena Cancer Center, Rome, Italy
Associate Professor, Department of Oncology, McMaster University, Canada

MicroRNAs expression is associated to resistance to PI3K inhibitors treatment in head & neck squamous cell carcinoma

2.00pm — **Cheryl Lee**

Senior Research Fellow, Endogenous Peptides Laboratory, Duke-NUS, Singapore

Micropeptide MOCCI and miR-147b encoded in C15orf48 coordinate to modulate infection outcomes

2.40pm — **End of Day 1**

3.00pm — **MiRXES Facilities Tour – by invitation only**

6.00pm — **Dinner – by invitation only**

Scientific Programme
21 September 2022, Wednesday

Morning Session

8.00am Registration

Theme: Preventive and Precision Health – ncRNA Biomarkers (II)
Chair: Dr Cheong Jit Kong
NUS Medicine, Singapore

8.30am **Peter Dedon**
Singapore Professor of Biological Engineering, Massachusetts Institute of Technology (MIT), USA
Lead Principal Investigator in the Singapore-MIT Alliance for Research and Technology Antimicrobial Drug Resistance IRG
New Sequencing And Mass Spectrometry Tools for Quantitative Analysis of the tRNome

9.00am **Nagaendran Kandiah**
Associate Professor of Neuroscience and Mental Health, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
Director, Dementia Research Centre, Singapore
The role of microRNA in the early detection of Alzheimer's Disease and Vascular Dementia

9.30am **Dennis Wang**
Head of Bioinformatics, A*STAR Singapore Institute for Clinical Sciences, Singapore
Professor in Data Science, National Heart and Lung Institute, Imperial College London, United Kingdom
Unsupervised Clustering of Pulmonary Hypertension Using Circulating miRNA - Towards A New Molecular Classification?

10.00am Morning Tea Break

Chair: Dr Tang Yew Chung
MiRXES Pte Ltd

10.20am **Takahiro Ochiya**
Professor, Department of Molecular and Cellular Medicine, Tokyo Medical University, Japan
Keynote Lecture: *Extracellular vesicles as a carrier of ncRNAs*

11.20am Lunch

Scientific Programme
21 September 2022, Wednesday

Afternoon Session

Theme: ncRNA – Therapeutics
Chair: Dr Yvonne Tay
NUS Medicine, Singapore

12.20pm **Vinay Tergaonkar**

Adjunct Professor, Department of Pathology and Department of Biochemistry, NUS Medicine, Singapore
Research Director, Institute of Molecular and Cell Biology, A*STAR, Singapore

An RNA:RBP interaction as a therapeutic vulnerability of wtIDH1 high-grade gliomas

12.50pm **Le Thi Nguyet Minh**

Assistant Professor, Department of Pharmacology, NUS Medicine, Singapore

Delivery of immunomodulatory RNAs using extracellular vesicles for anti-cancer immunotherapy

1.20pm **Wang Jiong-Wei**

Assistant Professor, Department of Surgery, NUS Medicine, Singapore
Principal Investigator, Nanomedicine Translational Research Program, NUS Medicine, Singapore

ncRNAs in Milk Extracellular Vesicles: oral therapeutics for gut inflammation and fatty liver disease

1.50pm **End of Day 2**

2.00pm **Networking – by invitation only**

Scientific Programme
22 September 2022, Thursday

Morning Session

8.00am Registration

Theme: Liquid Biopsy Summit
Chair: Dr Yong Wei Peng & Dr Iain Tan
National University Cancer Institute, Singapore
National Cancer Centre, Singapore

8.30am **Tony Mok**

Chairman, Department of Clinical Oncology, The Chinese University of Hong Kong, Hong Kong

Keynote Lecture: *The potential role of liquid biopsy for MRD monitoring of lung cancer*

9.30am **Chee Cheng Ean**

Assistant Professor, Department of Medicine, NUS Medicine, Singapore
Senior Consultant, Department of Haematology-Oncology, National University Cancer Institute, Singapore

Liquid biopsies in GI cancers

10.00am Morning Tea Break

10.20am **Goh Boon Cher**

Professor, Department of Pharmacology and Department of Medicine, NUS Medicine, Singapore
Deputy Director (Research), National University Cancer Institute, Singapore

Circulating extracellular vesicles (EVs) as intercellular communicators and potential for cancer diagnostics

10.50am **Samantha Yang Peiling**

Assistant Professor, Department of Medicine, NUS Medicine, Singapore
Senior Consultant, Division of Endocrinology, National University Hospital, Singapore

Utility of Liquid Biopsy in Thyroid Cancer

11.20am Lunch

Scientific Programme
22 September 2022, Thursday

Afternoon Session

Theme: Precision Health – Emerging Technologies
Chair: Dr Jan Heng
BIDMC, United States

12.20pm **Wan Yue**

Principal Investigator, RNA Structuromics Laboratory, A*STAR Genome Institute of Singapore, Singapore
Adjunct Assistant Professor, Department of Biochemistry, NUS Medicine, Singapore

Defining cellular identities through single cell RNA structure

12.50pm **Holger Heyn**

Team Leader, Single Cell Genomics Unit, Centre for Genomic Regulation (CNG), Spain

Single Cell Genomics for Precision Oncology

1.40pm **Cloud Paweletz**

Head of Research, Belfer Centre for Applied Cancer Science, Dana-Farber Cancer Institute (DFCI), United States

Leveraging the quantitative nature of cfDNA for cancer care

2.10pm ***Closing Remark***
Jimmy So

Co-chair, NUS ncRNA Symposium and Liquid Biopsy Summit 2022
Professor, Department of Surgery, NUS Medicine, Singapore

2.20pm End of Day 3

2.30pm Networking – by invitation only

Guests-of-Honour

Dr Chng Wee Joo

Vice-Dean (Research)
NUS Yong Loo Lin School of Medicine, Singapore

Provost's Chair Professor
NUS Department of Medicine, Singapore

Biography

Professor Chng Wee Joo is Director of the National University Cancer Institute, Singapore and Group Director of Research, at the National University Health System. He is a Provost's Chair Professor and Vice-Dean of Research of the Yong Loo Lin School of Medicine, and Senior Principal Investigator of the Cancer Science Institute of Singapore, at the National University of Singapore.

He is a member of many international professional committees, such as the International Myeloma Working Group and the Asian Myeloma Network. He is also involved in a number of Grant Review Committees, Conference Organising Committee, Advisory Boards and Steering Committees of Global Clinical Trials. He has authored more than 300 publications in many reputed journals, and actively participates in clinical trials and has delivered talks in many national and international conferences. He has won multiple awards for his outstanding achievements in translational research both locally and internationally including the NUHS Research Excellence Award, the International Myeloma Foundation's Brian GM Durie Outstanding Achievement Award, the National Medical Excellence Outstanding Clinician Scientist Award, the National Medical Research Council Senior Translational Research (STaR) Award, the National University of Singapore Young Researcher Award, and the Celgene Future Leaders in Haematology Award.

Dr Yeoh Khay Guan

Chief Executive
National University Health System, Singapore

Professor
Department of Medicine, NUS Yong Loo Lin School of Medicine, Singapore

Biography

Dr Yeoh Khay Guan is Professor of Medicine at the National University of Singapore. His concurrent appointments include Senior Vice President (Health Affairs) of the National University of Singapore, as well as Chief Executive of the National University Health System. He practices as a Senior Consultant at the Division of Gastroenterology and Hepatology, National University Hospital.

Dr Yeoh's research interest is in enhancing the early detection of gastric and colorectal cancers. He is the Lead Principal Investigator of the Singapore Gastric Cancer Consortium, a national flagship research group, and chairs the National Colorectal Cancer Screening Committee of the Health Promotion Board, Ministry of Health. He has published over 195 peer-reviewed papers in international journals and has an H-index of 57 with over 10,643 citations. He was awarded the National Medical Excellence Award as Outstanding Clinician Scientist by the Ministry of Health, Singapore in 2013.

NUS ncRNA Symposium &

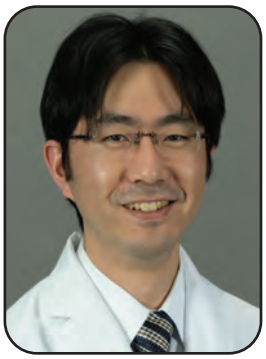
Liquid Biopsy Summit

Day 1

20 September 2022

Dr Tatsuro Murano

Associate Professor
Department of Gastroenterology and Endoscopy
National Cancer Center Hospital East (NCCHE), Japan



Biography

Dr Tatsuro Murano, Ph.D., is an Associate Professor in the Department of Gastroenterology and Endoscopy at the National Cancer Center Hospital East (NCCHE) of Japan. After receiving his M.D. from the Tokyo Medical and Dental University of Japan, he went on to study his Ph.D. at the university's Department of Gastroenterology and Hepatology. Subsequently, he joined the Massachusetts General Hospital in Boston, U.S.A., as a research fellow in their Center for Computational and Integrative Biology. In 2016, he returned to Tokyo Medical and Dental University to work as a clinical fellow in Gastroenterology and Hepatology. Now based in NCCHE, Chiba, Japan, as an attending staff for the Department of Gastroenterology and Endoscopy, he is involved in research involving the gastrointestinal track, such as pilot studies regarding detection of gastric cancer in the Japanese population.

Diagnostic performance of GASTROClear for detecting gastric cancer in the Japanese population

Aim: There is an unmet need for a non-invasive blood test that enables risk stratification of gastric cancer (GC) in Japan. We conducted a pilot study to evaluate the diagnostic performance of GASTROClear for detecting GC in the Japanese population.

Methods: Blood samples from 105 GC patients and 126 healthy controls (HC) were prospectively collected at two institutions and were subjected to GASTROClear assay followed by the risk score (G-score) evaluation. The diagnostic performance of G-score as well as anti-HP antibody, CEA and CA19-9 was assessed.

Results: The clinicopathological characteristics of GC cases was Stage (AJCC): 0-I/II-IV 62/43 (59/41%), 63 (60%) asymptomatic cases, histological type: tub1-tub2/por-sig-muc/others 57/44/4 (54/42/4%). AUC value for GC of G-score, anti-HP antibody, CEA and CA19-9 was 0.78, 0.78, 0.66 and 0.51, respectively. The sensitivity and specificity of G-score for GC were 77% and 63%, respectively. The sensitivity according to the clinicopathological characteristics was 69% in Stage 0/I and 88% in Stage II-IV, 83% in symptomatic cases and 73% in asymptomatic cases, 75% in histologically tub1-tub2 and 77% in por-sig-muc.

Conclusions: GASTROClear yielded a competent diagnostic ability for GC in the Japanese population and has a potential to contribute to efficient stratification for the risk of GC.

Dr Jan Heng

Assistant Professor
Department of Pathology,
BIDMC, Harvard Medical School, USA

Biography

Dr Heng is an Assistant Professor of Pathology at Beth Israel Deaconess Medical Center (BIDMC), an affiliate of Harvard Medical School. She conducts translational breast cancer research, in particular, to develop clinically relevant modalities. A native of Singapore, she completed her undergraduate and PhD studies in Australia, and trained at the University of Toronto, Canada, and at BIDMC before becoming a principal investigator.

She is part of the The Cancer Genome Atlas breast cancer working group, is a long-time collaborator of the Nurses' Health Study for molecular pathology epidemiology research, and leads the BIDMC transgender breast working group.

Plasma miRNAs associated with cisplatin sensitivity in breast cancer

Background. Breast cancer is the second most common cancer in women. Developing biomarkers to predict whether a patient is likely to respond to a particular treatment will reduce breast cancer morbidity and mortality. We leveraged the two-arm, randomized Phase II INFORM trial (NCT01670500) to investigate if plasma miRNAs are associated with complete pathological response (pCR; primary outcome) or residual cancer burden (RCB; secondary outcome) in patients who received either neoadjuvant cisplatin monotherapy or doxorubicin plus cyclophosphamide (AC).

Methods. We screened 100 pre-treatment plasma samples for 352 miRNAs. After quality control and data pre-processing, 3 samples and 101 miRNAs detected in <10% of samples were excluded. Binary logistic regression was used to identify miRNAs associated with pCR in patients who received cisplatin (n=53) or AC (n=44).

Results. Eight miRNAs were associated with pCR and 18 miRNAs were associated with RCB in the cisplatin arm ($p<0.01$ and FDR <0.25). No miRNA was associated with pCR or RCB in the AC arm.

Conclusions. Plasma miRNAs may reflect unique tumor characteristics or patient's immune response that confer cisplatin sensitivity. The validation of this finding using plasma samples from our sister trial (NCT01982448) is ongoing.

Dr Frank Slack

Director
Harvard Medical School Initiative for RNA Medicine,
BethIsrael Deaconess Medical Center, USA

Shields Warren Mallinckrodt Professor
Department of Pathology,
Harvard Medical School, USA

Biography

Dr Frank Slack, Ph.D., is Director of the Harvard Medical School Initiative for RNA Medicine hosted at Beth Israel Deaconess Medical Center (BIDMC). He is also the Shields Warren Mallinckrodt Professor of Pathology at Harvard Medical School. He received his B.Sc. from the University of Cape Town in South Africa, before completing his Ph.D. in molecular biology at Tufts University School of Medicine. He started his work on microRNAs as a postdoctoral fellow in Gary Ruvkun's laboratory at HMS. Dr. Slack subsequently moved to the Department of Molecular, Cellular, and Developmental Biology at Yale University, where he was a program leader in the Yale Cancer Center and the director of the Yale Center for RNA Science and Medicine. There he discovered that microRNAs regulate key human oncogenes and have the potential to act as therapeutics. He also demonstrated the first role for a microRNA in the aging process. In 2014, he joined Harvard Medical School/BIDMC. In 2016 he became the founding Director of the HMS Initiative in RNA Medicine. In 2020 he took on the role of Director of the BIDMC Cancer Research Institute. Dr. Slack was an Ellison Medical Foundation Senior Scholar; received the 2014 Heath Memorial Award from MD Anderson Cancer Center and is an NCI Outstanding Investigator. He is co-founder of three companies in this area, MiraDx, Impilo and 28/7 Rx, and is or has been on the SAB of multiple additional companies, including Mirna Rx, miRagen Rx, Alexion Pharmaceuticals, The RNA Medicines Company.

Towards microRNA-based cancer medicine

MicroRNAs are small non-coding RNAs that regulate gene expression to control important aspects of development and metabolism such as cell differentiation, apoptosis and lifespan. miR-21, miR-155, let-7 and miR-34 are microRNAs implicated in human cancer. Specifically, human let-7 and miR-34 are poorly expressed or deleted in lung cancer, and over-expression of let-7 or miR-34 in lung cancer cells inhibits their growth, demonstrating a role for these miRNAs as tumor suppressors in lung tissue. let-7 and miR-34 regulate the expression of important oncogenes implicated in lung cancer, suggesting a mechanism for their involvement in cancer. We are focused on the role of these genes in regulating proto-oncogene expression during development and cancer, and on using miRNAs to suppress tumorigenesis. In contrast, miR-21 and miR-155 are oncomiRs and up-regulated in many cancer types. We are also developing effective strategies to target these miRNAs as a novel anti-cancer approach. Lastly, we are examining the non-coding portions of the genome for mutations and variants that are likely to impact the cancer phenotype. We have successfully resequenced the 3'UTRome and microRNAome from cancer patients, including those with a family history of cancer to identify the next generation of cancer biomarkers and targets.

Dr Polly Chen
Associate Professor
Department of Anatomy, NUS Medicine, Singapore

Principal Investigator
Cancer Science Institute, Singapore

Biography

Dr Polly Leilei Chen got her Bachelor of Medicine in 2002 from Jiangsu University, China, followed by a 2-year specialized training program in Obstetrics & Gynaecology. In 2006-2012, she completed her PhD in Cancer Genetics in Professor Xin-Yuan Guan's laboratory at the University of Hong Kong and had her postdoctoral training in the same laboratory. In 2014, Dr Chen joined National University of Singapore (NUS) as an Assistant professor in the Department of Anatomy and Principal Investigator at Cancer Science Institute of Singapore. Dr Chen currently places her research focus on functional and mechanistic investigation of RNA changes leading to cancer initiation, relapse post treatment, and drug resistance; and understanding how pre-neoplastic and tumour cells develop immune evasion mechanisms through impairing RNA sensing and immune activation.

Noncoding natural antisense transcripts (ncNAT) Influence Promoter Usage of Their Counterpart Sense Genes in Cancer

Multiple noncoding natural antisense transcripts (ncNAT) are known to modulate key biological events such as cell growth or differentiation. However, the actual impact of ncNATs on cancer progression remains largely unknown. We recently identified a complete list of differentially expressed ncNATs in hepatocellular carcinoma. Among them, a previously undescribed ncNAT HNF4A-AS1L suppressed cancer cell growth by regulating its sense gene HNF4A, a well-known cancer driver, through a promoter-specific mechanism. RNA sequencing (RNA-seq) data from 23 tissue and cancer types identified approximately 100 ncNATs whose expression correlated specifically with the activity of one promoter of their associated sense gene. Our results demonstrate that promoter-specific regulation is a mechanism used by ncNATs for context-specific control of alternative isoform expression of their counterpart sense genes.

Dr Yvonne Tay

President Assistant Professor
Department of Biochemistry, NUS

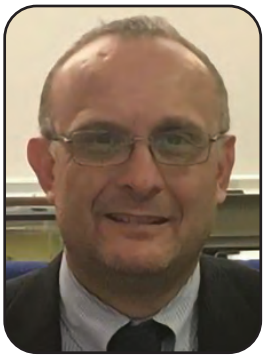
Principal Investigator
Cancer Science Institute of Singapore, NUS

Biography

Dr Yvonne Tay began her research career in Bing Lim's lab at the Genome Institute of Singapore, where she studied miRNA function and mechanisms of action (Tay et al, Nature 2008). She then pursued her postdoctoral training in the Pandolfi lab at Harvard Medical School, where she investigated how transcripts can co-regulate each other by competing for shared miRNAs (Tay et al, Cell 2011). Now based at the Cancer Science Institute of Singapore and National University of Singapore, Yvonne's research group studies non-coding RNAs as well as the non-coding regions of protein-coding mRNAs (untranslated regions, UTRs). As many mRNA populations comprise transcripts with different UTRs, and these UTRs control key processes such as stability, localization and transport, a better understanding of their function may lead to insights into the regulation of key cancer genes.

Widespread 3'UTR splicing promotes oncogene expression and tumorigenesis

Most mammalian genes generate messenger RNAs with variable untranslated regions (UTRs) which are important post-transcriptional regulators. In cancer, 3'UTR shortening via alternative polyadenylation can activate oncogenes. However, 3'UTR splicing remains poorly understood as splicing studies have traditionally focused on protein-coding alterations. Here, we systematically map the pan-cancer landscape of 3'UTR splicing. We find that 3'UTR splicing is widespread, upregulated in cancers, correlated with poor prognosis and more prevalent in oncogenes. Targeted inhibition of 3'UTR splicing efficiently reduces oncogene expression and impedes tumor progression. Notably, we identify CTNNB1 3'UTR splicing as the most consistently dysregulated event across cancers and demonstrate that its spliced 3'UTR variant is the predominant contributor to its oncogenic functions. Overall, our study provides the first compendium of 3'UTR splicing in cancer and may launch new avenues for RNA-based anti-cancer therapeutics.



Dr Giovanni Blandino

Director
Translational Oncology Research Unit,
Regina Elena Cancer Center, Rome, Italy

Associate Professor
Department of Oncology,
McMaster University, Canada

Biography

Dr Giovanni Blandino obtained his M.D. from the Medical School University of Catania, Italy, specialized in Molecular Oncology during residency at the University of Milan, and completed his postdoc fellowship at the Weizmann Institute of Science, Israel. In 2022, he was appointed as Director of the Translational Oncology Research Unit at the Regina Elena Cancer Center, Rome, while holding multiple appointments as Associate Professor of Oncology at McMaster University, Canada, and Translational Research Coordinator for Clinical Studies at the Regina Elena Cancer Institute, Rome, Italy. He has held several Editorial Board positions, such as being Deputy Editor for the Journal of Experimental and Clinical Cancer Research (JECCR) with a latest IF of 12.658, and since 2020, he has been invited to at least 25 reviews, commentaries, and editorials. His research focuses on the oncogenic role of mutant p53 proteins and the translational implications of small non-coding RNAs as epigenetic biomarkers relating to cancer stratification, early detection, and prediction of treatment response.

MicroRNAs expression is associated to resistance to PI3K inhibitors treatment in head & neck squamous cell carcinoma

Head and neck squamous cell carcinomas (HNSCCs) frequently harbor alterations in the PI3K signaling axis and, particularly, in the PIK3CA gene. The promising idea of using PI3K inhibitors for the treatment of HNSCC has, however, clashed with a spontaneous development of resistance over time, observed both in PDX models and cell lines. We previously reported that an efficient response to alpelisib, a PI3Kα-selective inhibitor, relies on the decrease of c-Myc transcriptional activity in HNSCC cells. Accordingly, development of resistance to alpelisib is accompanied by c- Myc hyperactivation.

By analyzing a cohort of 18 HNSCC PDX models, treated or not with alpelisib, including 12 responding and 6 non-responding PDXs, we identified members of miR-17-92 cluster that are induced by alpelisib treatment and are responsible for inhibition of PTEN expression specifically in non-responding PDXs. Of note, both PTEN knock-out or down-regulation confer resistance to treatment with alpelisib in HNSCC cells. Mechanistically, active c-Myc is recruited on MIR17HG promoter in alpelisib-resistant cells, causing the sustained expression of the miR-17-92 cluster. Accordingly, blocking of c-Myc or miR-17-92 members causes induction of PTEN and increases the response to alpelisib in HNSCC cells.

Of note, profiling of baseline circulating miRNAs in the same HNSCC PDX cohort allowed identifying a panel of miRNAs discriminating responding from non-responding PDXs.

Altogether, these results highlight the relevance of miRNAs in establishing resistance to alpelisib and in predicting alpelisib response in HNSCC.

Dr Cheryl Lee

Senior Research Fellow
Endogenous Peptides Laboratory, Duke-NUS, Singapore

Biography

Dr Cheryl Lee is a senior postdoc in the endogenous peptide lab in Duke-NUS Medical School, under the supervision of Asst Prof Lena Ho. She received her PhD from University of Cambridge, working on reproductive biology. During her PhD, she characterised the stem cell niche of placental cells and carried out a screen to identify factors that improve the stemness of trophoblast stem cells. When she returned to Singapore, she switched to studying vascular inflammation, as it is the leading cause of cardiovascular diseases. Through a screen to search for novel peptides involved in inflammation, she discovered a micro-peptide that controls the ETC, called MOCCI. Now her research centres around understanding how the ETC controls inflammation, particularly during viral infection.

Micropeptide MOCCI and miR-147b encoded in C15orf48 coordinate to modulate infection outcomes

Chronic vascular inflammation is implicated in many cardiovascular diseases, notably atherosclerosis. Ribosome profiling is a powerful tool to identify small open reading frame-encoded peptides (SEPs), many of which were previously ignored due to their size. Using ribosome profiling and RNA-sequencing of human aortic endothelial cells (HAECs), we have identified novel SEPs upregulated during vascular inflammation, termed VI-SEPs. Here, we report the discovery and deorphanization of Modulator of Cytochrome C oxidase during Inflammation (MOCCI), a 83 aa mitochondrial SEP (mito-SEP) that is specific to the inflamed state. MOCCI is a paralog of NADH:Ubiquinone Oxidoreductase Complex Assembly Factor 4 (NDUFA4), the 14th subunit of the mitochondrial respiratory chain Complex IV (CIV). During inflammation, MOCCI replaces NDUFA4 in CIV, which leads to repressed CIV activity, lower membrane potential and reduced ROS production. Interestingly, the transcript of MOCCI also contains a miRNA, miR-147b that targets NDUFA4 transcript for degradation, thereby enforcing the MOCCI-to-NDUFA4 switch. miR-147b targets other genes beyond NDUFA4, resulting in MOCCI and miR-147b playing convergent and divergent roles during inflammation. Together, MOCCI and miR-147b coordinate to protect the host during infection and inflammation.

NUS ncRNA Symposium &

Liquid Biopsy Summit

Day 2

21 September 2022

Dr Peter Dedon

Singapore Professor
Biological Engineering,
Massachusetts Institute of Technology (MIT), USA

Lead Principal Investigator
Singapore-MIT Alliance for Research and Technology
Antimicrobial Drug Resistance IRG

Biography

Dr Peter Dedon is the Singapore Professor of Biological Engineering at MIT and the Lead Principal Investigator in the Singapore-MIT Alliance for Research and Technology Antimicrobial Drug Resistance IRG. With a focus on RNA and DNA biology, his group developed analytical and informatic platforms for basic and translational research in epigenetics, epitranscriptomics, and genetic toxicology in infectious disease and cancer. For the epitranscriptome – the dozens of modified ribonucleosides in all forms of RNA – his team has developed systems-level analytical tools to discover a mechanism of translational regulation of gene expression that links stress-specific reprogramming of 40-50 different tRNA modifications with selective translation of codon-based gene families essential for survival or phenotypic change. Pete and colleagues are leveraging these discoveries to develop new enzymatic tools for biotechnology, new methods for industrial microbiology and protein production, and novel antimicrobial agents and biological therapeutics.

New Sequencing and Mass Spectrometry Tools for Quantitative Analysis of the tRNome

The Central Dogma defines the "what" of biology: genes are transcribed into messenger RNAs that are translated into proteins. But it says nothing about the "when" or "how much" of expressing 20,000 genes in humans. Using convergent technologies, we discovered an information-rich scheduling system for translational regulation of gene expression involving the dozens of chemical modifications of RNA in every cell – the epitranscriptome. This mechanism involves stress-induced reprogramming of dozens of tRNA modifications to facilitate selective translation of codon-biased mRNAs critical to the cell stress response. Here we present three new tools for systems-level analysis of the tRNAome and translational regulation of gene expression: genome-wide codon analytics, high-throughput tRNA isolation and epitranscriptome analysis applied to the 5,800-strain *Pseudomonas aeruginosa* knockout library, and mass spectrometry-based RNA sequencing and modification mapping. We are leveraging these tools and discoveries to develop biomarkers of disease and novel therapeutics.

Dr Nagaendran Kandiah

Associate Professor
Neuroscience and Mental Health,
Lee Kong Chian School of Medicine, NTU, Singapore

Director
Dementia Research Centre, Singapore

Biography

Dr Nagaendran Kandiah is Associate Professor of Neuroscience and Mental health at LKCMedicine-NTU Singapore. He is the Director of the Dementia Research Centre (Singapore) and co-Director of the LKCMedicine Neuroscience & Menatal Health Programme. As a cognitive neurologist, he has a special interest in the diagnosis and management of mild cognitive impairment as well as young-onset dementia. Prof Kandiah also holds a clinician-scientist position with NMRC Singapore.

He has published over 150 peer-reviewed papers in the field of cognitive neuroscience and has received over 25 million dollars in research funding support. His current research projects investigate upstream mechanisms that cause dementia among Asians with a focus on small vessel cerebrovascular disease and blood brain barrier pathology.

The role of microRNA in the early detection of Alzheimer's Disease and Vascular Dementia

Increasing evidence suggests the need for early detection and timely intervention of Alzheimer's (AD) and Vascular Dementia (VaD). Detection of AD and VaD before the stage of extensive neurodegeneration will allow for disease modifying interventions of upstream pathology such as amyloid-ß, phospho-tau and blood brain barrier (BBB) dysfunction.

Existing diagnostic modalities for AD include costly PET imaging and/or invasive lumbar punctures to enable analyses of cerebrospinal fluid. There is a need for blood-based biomarkers to allow for widespread and timely detection of AD and VaD. In this regard, microRNA sequencing may offer novel diagnostic markers for AD and VaD. In this presentation, the current state of microRNA for the diagnosis of AD and VaD will be presented. Work from our group which evaluated identification of novel microRNAs for AD from peripheral mononuclear cells and cross validated using cerebrospinal amyloid-ß will be shared. The strategy to identify novel miRNA to detect BBB leakage in Asian patients with VaD will also be discussed.

The use of miRNA for early detection and for furthering research into pathobiology of AD and VaD can transform care models as well as allow for discovery of novel treatment targets for these major public health diseases.

Dr Dennis Wang

Head of Bioinformatics
A*STAR Singapore Institute for Clinical Sciences, Singapore

Professor in Data Science
National Heart and Lung Institute,
Imperial College London, United Kingdom

Biography

Dr Dennis Wang is an interdisciplinary researcher at the intersection of genomics, computer science and medicine. He is a Professor in Data Science at the National Heart and Lung Institute of Imperial College London and the Head of Bioinformatics at the A*STAR Singapore Institute for Clinical Sciences. He also holds honorary faculty appointments at the Universities of Sheffield, Liverpool and the National University of Singapore. His research focuses on using high-dimensional -omics data and artificial intelligence (AI) to understand multiple long-term health outcomes in population and disease cohorts. Having worked in both academia and industry, he enjoys mentoring junior bioinformaticians and clinicians interested in integrating patient data. Dennis obtained his Bachelor of Science in Computer Science, Microbiology and Immunology from The University of British Columbia, and both of his MPhil in Computational Biology and PhD in Biostatistics from the University of Cambridge.

Unsupervised Clustering of Pulmonary Hypertension Using Circulating miRNA - Towards A New Molecular Classification?

Pulmonary hypertension (PH) covers a broad spectrum of diseases with a variety of pathobiological mechanisms, phenotypes and aetiologies. The current clinical classification is based on invasive haemodynamics and disease aetiology categorised by 5 groups. Classification of patients into Group 1, 2 or 3 (pulmonary arterial hypertension, left heart disease and lung disease) based on clinical features can be challenging, with patients often falling into a 'grey area' that can result in inappropriate or missed treatment. We have previously demonstrated transcriptomic clusters of patients with idiopathic PAH and now hypothesize that unbiased molecular classification of patients with PH Group 1, 2 or 3 will identify patients with shared molecular profiles agnostic to the current clinical classification that may inform the best treatment choice. Serum samples from 786 patients with PH Group 1-3 from multiple sites were assayed for 600 microRNAs by MiRXES (Singapore). Unsupervised machine learning approach (spectral clustering) was used to identify stable miRNA-based subgroups of PH, and correlated with clinical phenotypes. Distinct microRNA signatures were defined for each of the clusters. Clusters contained common enriched pathways and five of the six clusters also contained uniquely enriched pathways (by miRNA targeting) suggesting some cluster specific mechanisms.

Dr Takahiro Ochiya

Professor
Department of Molecular and Cellular Medicine,
Tokyo Medical University, Japan

Biography

Dr. Takahiro Ochiya is a Professor of Department of Molecular and Cellular Medicine at Tokyo Medical University, Tokyo since 2018. After he got Ph.D. in 1988 in Osaka University and then went to do a post-doc at La Jolla Cancer Research (SF Burnham Institute for Medical Research), CA, USA. During his carrier at National Cancer Center (1993~2018), Tokyo, Dr. Ochiya's lab focused the development of novel animal models, methods, and strategies to study cancer development and metastasis. Especially, current focuses are non-coding RNA-based novel cancer diagnosis and therapeutics. Dr. Ochiya is one of top scientist in Exosome (EV) research and carries President of Japanese Society of Extracellular Vesicles (JSEV) since 2014 and a board member of ISEV. Dr. Ochiya is recipients of HCR (highly cited researchers) in 2019, 2020, and 2021 by Web of Science.

Extracellular vesicles as a carrier of ncRNAs

Liquid biopsy is expected to be a promising cancer screening method because of its low invasiveness and the possibility of detecting multiple types in a single test. In the last decade, many studies on cancer detection using ncRNAs such as microRNAs (miRNAs) in blood have been reported. Several studies suggest that miRNAs can detect even early-stage cancers with high sensitivity, and it is expected that miRNAs will be useful as an early cancer screening test. However, issues remain for miRNA-based multiple cancer type screening tests. First, the possibility of identifying cancer types by collecting samples from multiple facilities has not been determined. Second, there have been reports that ncRNAs specific to cancer types have been identified, but the variety of ncRNAs is not consistent among reports. To put small RNA tests into practical use as a multiple cancer type screening test, it is necessary to develop a method that can be applied to multiple facilities. Here we will discuss on our current experiences on miRNA cancer test as well as development of EV-based novel cancer biomarkers.

Dr Vinay Tergaonkar

Adjunct Professor
Department of Pathology and Department of Biochemistry,
NUS Medicine, Singapore

Research Director
Institute of Molecular and Cell Biology, A*STAR, Singapore

Biography

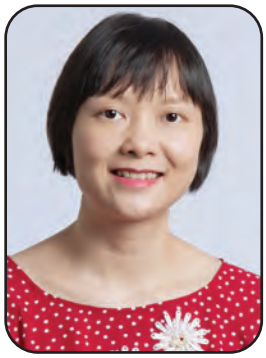
Dr Vinay Tergaonkar obtained his Ph.D. (2001) from NCBS Bangalore, through an international cancer society (UICC) fellowship for collaborative research at Tufts University, Boston, USA. He has been a fellow (2001-2004) and a special fellow (2004-present) of the Leukemia and Lymphoma Society of America and conducted his postdoctoral studies at the Salk Institute for Biological Studies, La Jolla, California. He currently serves as Research Director at Institute for Molecular and Cell Biology (IMCB), Singapore, and a Professor at School of Medicine at National University of Singapore. He serves on Editorial Boards of 1) Science Advances (AAAS), 2) Molecular and Cellular Biology (American Society for Molecular Biology), 3) Biochemical Journal (Portland Press). Work from his lab has received international recognition including the British council development award (2014), the Premiers' fellowship from Government of South Australia (2015) and University of Macau Distinguished Professorship (2019).

An RNA:RBP interaction as a therapeutic vulnerability of wtIDH1 high-grade gliomas

Wild-type IDH1 (wtIDH1) high-grade gliomas, especially glioblastomas (GBMs) are highly resistant to chemo- and immune therapies which target proteins. RNAs and RNA binding proteins (RBPs) have now been recognized as emerging targets for cancer therapy, but until now, targeting RNA:RBPs in wtIDH1 high-grade gliomas or any other cancer has not been successful. Using genomic, genetic and pharmacological methods, we identified a unique RNA:RBP; LOC:DHX15 complex as a selective genetic vulnerability in wtIDH1 GBMs. LOC:DHX15 itself regulated by wtIDH1 dependent chromatin in turn regulates the infiltration of glioma-associated microglia and macrophages (GAMs) which drive cancer progression and therapy resistance. Targeting LOC:DHX15 with brain penetrating small molecules synergizes with temozolomide (TMZ) to improve efficacy, specifically in wtIDH1 GBMs. This study reveals unexplored wtIDH1 high-grade glioma dependencies beyond proteins and suggests that targeting functional RNA:RBP interactions could be the way forward.

Dr Le Thi Nguyet Minh

Assistant Professor
Department of Pharmacology, NUS Medicine, Singapore



Biography

Dr Minh Le graduated from NUS with a Bachelor's degree in Life Sciences and a Ph.D. degree in Computational and Systems Biology, under the guidance of Prof. Bing Lim and Prof. Harvey Lodish. She was trained as a postdoctoral fellow with Prof. Judy Lieberman at Boston Children's Hospital for 5 years and worked at City University of Hong Kong as an Assistant Professor for 4 years before returning to NUS. Dr Le is well recognised for her contributions to the field of microRNAs, extracellular vesicles and cancer biology. Her group has recently developed a strategy to harness extracellular vesicles from red blood cells for delivery of RNA drugs. This drug delivery platform is the foundation for her start-up company, Carmine Therapeutics. She is also an associate/deputy editor of JEV and JExBio. She has recently received the NUS Alumni award, Falling Walls Venture, and Graduate Mentor of the Year award.

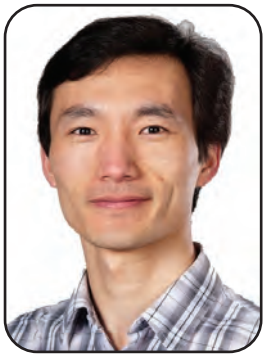
Delivery of immunomodulatory RNAs using extracellular vesicles for anti-cancer immunotherapy

RNA-based therapeutics have become one of the most promising new classes of medicine in recent years. However, the delivery of RNA drugs is still challenging. We have shown that red blood cell extracellular vesicles (RBCEVs) are the ideal carriers for therapeutic RNAs because RNAs can be loaded readily into the EVs and delivered to cancer cells at high efficiency. RBCEVs are nontoxic, nonimmunogenic and devoid of DNA. Moreover, RBCEVs can be produced in a large quantity from donated blood. Here, we describe new development of RBCEVs for the delivery of immunomodulatory RNAs (immRNAs) that acts as RIG-I agonists. We demonstrate that immRNA-loaded RBCEVs induce RIG-I cascade activation, type I IFN production, and immunogenic cell death in breast cancer cells. Intratumoral administration of immRNA in RBCEVs significantly suppresses tumor growth of mammary breast cancer, and induces immune cell infiltration and tumor cell apoptosis mediated by RIG-I activation, turning the 'cold' tumors 'hot'. Furthermore, we demonstrate that intrapulmonary delivery of immRNA-loaded RBCEVs modified with EGFR-targeting nanobodies actively enhances the potency of immRNA, leading to suppression of tumor metastasis and elevated tumor-specific immune responses in metastatic EGFR-positive breast cancer mouse models. Thus, delivery of RIG-I agonists using RBCEVs is a promising approach for anti-cancer immunotherapy.

Dr Wang Jiong-Wei

Assistant Professor
Department of Surgery, NUS Medicine, Singapore

Principal Investigator
Nanomedicine Translational Research Program,
NUS Medicine, Singapore



Biography

Dr Wang Jiong-Wei received his Ph.D. in Medicine in 2013 from the Leiden University Medical Centre (The Netherlands). After a brief postdoctoral training in the University Medical Centre Utrecht, he moved to the National University of Singapore (NUS). He was promoted to Assistant Professor in 2019 at the Department of Surgery, with joint appoints at the Department of Physiology and the Cardiovascular Research Institute, and currently is also a Principal Investigator in the Nanomedicine Translational Research Program, Yong Loo Lin School of Medicine, NUS. His current research interests focus on the preclinical development of nanotheronostics with natural and/or synthetic nanoparticular systems for the treatment of inflammatory and metabolic diseases.

ncRNAs in Milk Extracellular Vesicles: oral therapeutics for gut inflammation and fatty liver disease

Milk-derived extracellular vesicles (mEVs) have been emerging as novel therapeutic nanomaterials for intestinal inflammation, however, the impact of mEVs on intestinal barrier integrity in gut inflammation and associated metabolic disease remains unexplored. mEVs contain abundant bioactive non-coding RNAs, such as microRNAs. By KEGG pathway analyses, we found in this study that all the top 40 microRNAs in bovine mEVs were involved in signaling pathways related to intestinal barrier integrity and inflammation. Our further analysis revealed that most of those microRNAs were present in both bovine mEVs and human mEVs. This talk will discuss our recent preclinical studies exploring the therapeutic effects of mEVs in gut inflammation and fatty liver disease.

NUS ncRNA Symposium &

Liquid Biopsy Summit

Day 3

22 September 2022

Dr Tony Mok

Chairman, Professor
Department of Clinical Oncology,
The Chinese University of Hong Kong, Hong Kong

Biography

Dr Tony S.K. Mok was trained at the University of Alberta, Canada and he subsequently completed a fellowship in medical oncology at the Princess Margaret Hospital in Toronto. After working as a community oncologist in Toronto, Canada for seven years, he returned to Hong Kong in 1996 to pursue an academic career.

Dr Mok is the Li Shu Fan Medical Foundation endowed Professor and Chairman of Department of Clinical Oncology at The Chinese University of Hong Kong. His main research interest focuses on biomarker and molecular targeted therapy in lung cancer. He was the Principal Investigator and first author on the landmark IRESSA® Pan-Asia Study (IPASS), which was the first study that confirmed the application of precision medicine for advanced lung cancer. He has led and co-led multiple international phase III studies. These projects address various aspects on management of advanced lung cancer, and basically have defined the current practice.

The potential role of liquid biopsy for MRD monitoring of lung cancer

Risk of recurrence in patients with early resectable lung cancer continues to be substantial despite successful surgery. Microscopic residual cancer cells in lymphatic or circulation system are the primary seed and indication for future tumor recurrence. Being able to detect minimal residual disease (MRD) would help to select the high risk patients and to offer further intervention. Advancing sequencing technologies allow us to identify the intrinsic genomic anomalies that are specific to cancer, and develop a personalized liquid biopsy for detection of MRD. Abbosh et al (Nature 2017) performed exome sequencing on resectable lung cancer and constructed a phylogenetic tree. Based on which, they established a gene panel for detection of MRD by NGS of plasma cfDNA at follow up. Patients with positive MRD at follow-up almost always recur. We are still at early stage of development with MRD as a practical tool for management of resectable lung cancer. At this lecture we shall review the current data and future direction.

Dr Chee Cheng Ean

Assistant Professor
Department of Medicine, NUS Medicine, Singapore

Senior Consultant
Department of Haematology-Oncology,
National University Cancer Institute, Singapore

Biography

Dr Chee Cheng Ean currently practices as a senior consultant medical oncologist and clinician investigator in GI cancers. She also holds the Deputy Director (Clinical) position at the National University Cancer Institute, Singapore, and Assistant Professor, Yong Loo Lin School of Medicine, National University of Singapore. She graduated from University College London (UCL) Medical School, United Kingdom with a Bachelor of Science (Hons) in Tumour Biology and MB BS (London) and is board certified by the American Board of Internal Medicine (ABIM) in Internal Medicine (Mayo Clinic, USA), Medical Oncology (Mayo Clinic, USA) and Haematology (Mayo Clinic, USA). As a clinician investigator, her portfolio includes clinical and research initiatives in precision oncology and clinical trials involving novel therapeutics in GI cancers which have been awarded institutional and national grant funding. She is the current chair of the Singapore Cancer Society Colorectal Cancer Awareness Month Committee.

Liquid biopsies in GI cancers

There has been emerging data on the utility of liquid biopsies in GI cancers. Not only it is used as a surrogate for tissue, there may be additional predictive and prognostic value of liquid biopsies which may impact treatment decisions for patients. We will review the prevailing and upcoming liquid biopsy platforms in GI cancers and discuss where the technology may fit in the current treatment paradigm.

Dr Goh Boon Cher

Professor
Department of Pharmacology and Department of Medicine,
NUS Medicine, Singapore

Deputy Director (Research),
National University Cancer Institute, Singapore

Biography

Dr Goh Boon Cher is a physician scientist with interest in experimental therapeutics of cancer. He has extensive experience with conducting phase 1 clinical trials and clinical trials in head and neck and lung cancer at the National University Cancer Institute, Singapore. He is senior principal investigator at the Cancer Science Institute, where he leads a team of scientists in studying mechanisms of treatment resistance and exosomes as biomarkers of cancer.

Circulating extracellular vesicles (EVs) as intercellular communicators and potential for cancer diagnostics

Exosomes are 40-100nm membrane bound extracellular vesicles released from cells through fusion of multivesicular bodies and the plasma membrane, carrying proteins, nucleic acids and lipids. Transported by diffusion to surrounding tissues and cells, and circulating in the bloodstream, their contents can reveal important biological states, their cargo can mediate cellular effects when taken up by other cells. For example, cellular communication is possible through these circulating EVs. Therefore, isolation and analysis of these vesicles in blood is a rich source of biomarkers and can yield important diagnostic information.

In this session, to illustrate the potential of EV as potential diagnostic markers and transfer of biologically active molecules, an example of the methodology used to develop a lung cancer diagnostic biomarker based on proteomic analysis, and another on the functional significance of an EV cargo protein, ILEI/FAM3C, will be presented.

Dr Samantha Yang Peiling

Assistant Professor
Department of Medicine, NUS Medicine, Singapore

Senior Consultant
Division of Endocrinology,
National University Hospital, Singapore

Biography

Dr Yang obtained her medical degree and Masters of Medicine from the National University of Singapore (NUS) and the Royal College of Physicians, United Kingdom [MRCP (UK)]. She received her training in Endocrinology at National University Hospital, Singapore, followed by a thyroid cancer fellowship at Memorial Sloan Kettering Cancer Centre in New York, United States. She is on a research fellowship working on thyroid cancer re-differentiation in NUS.

Her research focuses on the utilisation of molecular tools for thyroid nodule evaluation, and the treatment and surveillance of thyroid cancer patients. She is studying mechanisms for upregulation of sodium-iodide symporter in thyroid cancer cell lines with the aim of using therapeutics to optimise the expression of these channels to enable better uptake of adjuvant radioactive iodine (RAI) in thyroid cancer. She is the principal investigator of a re-differentiation therapy clinical trial in RAI-refractory metastatic thyroid cancer patients.

Utility of Liquid Biopsy in Thyroid Cancer

The standard of care for thyroid cancer management is thyroid surgery and adjuvant radioactive iodine (RAI). There is a paucity of clinical tool that quantifies residual thyroid volume reliably for precise RAI dosing. Serum thyroglobulin (TG), tumour marker for thyroid cancer, can fail to detect recurrence due to issues of TG antibody interference with TG immunometric assay and reduced TG production in de-differentiated cancer.

We hypothesise that the quantity of thyroid-specific cell-free RNA (cfRNA) is indicative of amount of thyroid tissues. Biologically significant and highly expressed thyroid-specific targets from Human Protein Atlas and literature were selected and the plasma cfRNAs were quantifiable using qRT-PCR. We demonstrated the clinical relevance of circulating TPO cfRNA by tracking temporal changes in setting of peri-treatment, recurrence, and TG antibody positive state. Using a multiplex pre-amplification approach, the TPO cfRNA was a potential biomarker that can track residual thyroid mass. It can be further optimised for quantification of thyroid volume to guide RAI doses and for detection of recurrence.

Dr Holger Heyn

Team Leader
Single Cell Genomics Unit
Centre for Genomic Regulation (CNG), Spain

Biography

As leader of the Single Cell Genomics Team at the Spanish National Centre for Genomic Analysis (CNAG-CRG) and co-founder of Omniscope, Dr. Heyn focuses on the systematic integration of single-cell and spatial genomics data to elucidate causalities underlying diseases. His group combines technology development with research activities that center on cell atlasing projects and immuno-oncology. Dr. Heyn published 85 articles, resulting in an h-index of 52 (Google Scholar). The EU and the Chan Zuckerberg Initiative support Dr. Heyn's participation in the Human Cell Atlas (HCA) Project, where he leads the atlas of the B-cell lineage and contributes to the pancreas and the kidney atlases. He also co-chairs the HCA Standards and Technology Working Group. As Scientific Co-founder of OmniScope, Dr. Heyn brings high-resolution profiling technologies to clinical application, developing advanced diagnostics tools. OmniScope is a Systems Diagnostics company providing sensitive solutions to detect diseases early for interceptive medicine.

Single Cell Genomics for Precision Oncology

Single-cell and spatial RNA sequencing are at the forefront of techniques to chart molecular properties of individual cells. Recent methods are scalable to thousands of cells and high spatial resolution, enabling an unbiased sampling and in-depth data-driven characterization. To ensure high-quality data generation, we generated benchmark datasets to systematically evaluate techniques for their power to describe cell types and states comprehensively and to identify sampling biases that arise in large patient cohorts and biobanks. For translational immuno-oncology, we generated a Tumor Immune Cell Atlas through the integration of single-cell transcriptome data from 13 cancer types and >500,000 cells into a joint reference map. The atlas served as a reference for an automated cell annotation system for human tumors and mouse cancer models. To allow spatial mapping of immune cell states in tumor sections, we developed a computational framework to integrate spatial transcriptomic data with single-cell reference maps. Further, using advanced single-cell and ultra-high resolution T-cell receptor repertoire profiling of liquid biopsies, we showcase the live-tracking of tumor immune profiles in the blood and the cerebrospinal fluid, laying the ground for real-time patient monitoring.

Dr Wan Yue

Principal Investigator
RNA Structuromics Laboratory,
A*STAR Genome Institute of Singapore, Singapore

Adjunct Assistant Professor
Department of Biochemistry, NUS Medicine, Singapore

Biography

Dr Yue Wan received her B.Sc in Cell Biology and Biochemistry from the University of California, San Diego. She obtained her Ph.D in Cancer Biology from Stanford University, USA, under the mentorship of Howard Y. Chang. During her PhD, she developed the first high-throughput method for probing RNA structures genome-wide. Dr Wan is a recipient of the NSS-PhD scholarship from Agency for Science, Technology and Research (A*STAR) in Singapore, and is currently an Associate director in the domain Epigenetics and Epitranscriptomics Regulation in the Genome Institute of Singapore. She is a Society in Science- Branco Weiss Fellow, EMBO Young Investigator and CIFAR-Azrieli Global Scholar. Dr Wan is also a recipient of the Young Scientist Award and L'Oreal-UNESCO for Women in Science, Singapore National Fellowship. She is interested in studying functional RNA structures and understanding their roles in regulating cellular biology.

Defining cellular identities through single cell RNA structure

The identity of an individual cell is dependent on co/post-transcriptional regulation, much of which is regulated by RNA structure. However, current structure-probing strategies require millions of cells as starting material, hiding the extent of RNA structural variation and regulation in individual cells. Here, we developed DISCOS (Defining Identity of Single Cells Originating from Structures) to determine RNA structure and transcript abundance simultaneously in single cells. We applied DISCOS to neurogenesis from hESCs, and obtained structure information for thousands of RNAs. We confirmed that DISCOS is accurate and observed that 1) transcripts in one cell type can show large differences in their levels of structural similarity in single cells; 2) RNAs in hESCs are more structurally similar as compared to RNAs in differentiated cells; 3) structurally similar transcripts are associated with translation; 4) structurally varied regions are enriched in 3'UTRs and can be regulated by RBPs; 5) RNA structure can be used to better define cellular identities. We also identified a structurally variable region in helix 44 of 18S rRNA that is associated with translation. DISCOS is readily applicable to other biological systems to illuminate the role of RNA structures in determining cellular identity and gene regulation in single cells.

Dr Cloud Paweletz

Head of Research
Belfer Centre for Applied Cancer Science,
Dana-Farber Cancer Institute (DFCI), USA

Biography

Dr. Paweletz is head of the research of the Belfer Center for Applied Cancer Science at the Dana Faber Cancer Institute (DFCI) in Cambridge, Massachusetts where he uses his experience in industry, government institutions and academia to translate innovative and novel discoveries into clinical trials at DFCI. Dr. Paweletz has invented and patented technologies in the fields of precision immunotherapy, molecular diagnostics, liquid biopsies, and proteomics. He joined from Merck & Co., Inc., where he most recently served as principal scientist, externalization lead, and proteomics site lead for the Department of Molecular Biomarkers. Prior to that, he was a postdoctoral fellow in the Department of Physiology at the Uniformed Services University School of Medicine in Bethesda, Maryland and a research fellow in the Laboratory of Pathology at the National Cancer Institute, National Institutes of Health (NIH). Dr. Paweletz earned his PhD with honors from Georgetown University and his Bachelor of Science Degree from Baldwin Wallace College.

Leveraging the quantitative nature of cfDNA for cancer care

The widespread establishment of precision therapies has ushered a new paradigm in cancer care over the last decade. There are now dozens of precision therapies used for different cancer types, with the biggest impact in non-small cell lung cancer (NSCLC) with drugs approved for mutations in at least 5 genes (RET, EGFR, ALK, ROS1, BRAF) and emerging therapies for several more gene. Fueled by technical innovation, plasma genotyping approaches (also known as “liquid biopsies”) now permit assessment of fundamental NSCLC genotypes rapidly using simple blood draws with several assays tests approved by the FDA, and others commonly reimbursed by payors. Additional strategies are now under investigation to increase sensitivity for early-stage disease and classify the site from which the cancer originated, such as by combining measurement of mutant cell-free DNA with protein-based biomarkers, methylation patterns, or miRNA. Here we present our institutional experiences implementing liquid biopsies and discuss lessons learned. The realization of these lessons, however, in turn spur significant investment in techniques and technologies to increase specificity and sensitivity, reduce the turnaround time, and cost for further clinical adoption of this promising diagnostic.

Notes

Contact Us

ncRNA
CORE@NUS

National University of Singapore
Department of Biochemistry
8 Medical Drive
MD7, Level 3, Benches 16-18
Singapore 117596

ncRNAcore@nus.edu.sg