

Issue 9 | Oct - Dec 2023





N2CR researchers featured on **Channel 5 News!**



N2CR Researchers Dr Leong Sai Mun and A/Prof Mikael Hartman shared about the discovery of altruistic behaviour in cancer cells, specifically breast cancer cells on Singapore's Channel 5 news on 23 Dec 2023. They appear from the 1.27min mark. Click here to watch!

DR DENNIS KAPPEI WINS EMBO GLOBAL INVESTIGATOR AWARD

EMBO Global Investigator Network is an initiative that enables excellent early-stage group leaders based in Chile, India, Singapore, and Taiwan to access a wide range of collaboration, networking, and training activities. Congrats to Dr Kappei on being one of the 10 new members!

Welcome to our



A/Prof Peter Goon Department of Medicine, NUS

new memberi





N2CR Functional Precision Medicine Asia Symposium 2023 On 14 November 2023, N2CR hosted the N2CR Functional Precision Medicine Asia Symposium 2023. We had the privilege of having Professor Anthony Letai, President of the Society for Functional Precision Medicine, as our guest of honour. As part of his opening address, Prof Letai spoke about the progress precision medicine has made and how new technologies are

opening up more avenues for exploration and research.

target identification as well as treatment prediction.

N2CR is proud to kick off the first Asia based event by bringing together leaders in the field of functional precision medicine to discuss how various functional readouts can result into better

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HERE'S WHAT'S UP!

Latest News

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February

• CanCycle 2023 2nd **Edition closing** ceremony

 N2CR Staff Retreat 2024 Follow us on social media!





Awardees of —•
The Distinguished Senior Clinician Award 2023

This award from the Ministry of Health, recognises role models among specialists in the public sector who have made exemplary contributions in clinical practice, education and research. Congratulations to Prof Goh Boon Cher and A/Prof Koh Liang Piu on being honoured for their tireless contributions to the field of medicine.

Prof Goh Boon Cher A/Prof Koh Liang Piu



To Prof Allen Yeoh On his promotion to full Professor!



Congratulations ! To A/Prof Yvonne Tay On her promotion to Associate Professor!

Research News (Oct - Dec 2023)

Transcriptional repression by a secondary DNA binding surface of DNA topoisomerase I safeguards against hypertranscription

(Nature Communications , Lau, M.S., Hu, Z., Zhao, X. et. al.)

A team of scientists, led by N2CR member Dr. Tee Wee Wei, has identified the enzyme DNA topoisomerase I (TOP1) as a key regulator of gene activity crucial for normal development and health. Their discovery reveals that a specific disease-associated mutation (R548Q) in TOP1 accelerates gene activity, disrupting normal developmental programs. Tight control of gene activity is essential, as dysregulation can contribute to diseases, particularly in aggressive cancers characterized by transcriptional overdrive. Importantly, the mutation does not impact TOP1's primary enzymatic function but hinders its ability to bind to DNA correctly. This research highlights TOP1 as a molecular rheostat, ensuring precise control of gene activity levels and maintaining appropriate total transcription levels in our cells.



Read More

Alterations to DNA methylation patterns induced by chemotherapy treatment are associated with negative impacts on the olfactory pathway

(Breast Cancer Research, Ho, P.J., Khng, A.J., Tan, B.KT. et. al.)



Exposure to chemotherapy can change "chemical tags" in our DNA. These tags don't change the actual DNA, but they can affect how easily the information on DNA is read and used. In a study with 125 breast cancer patients, researchers found 141 regions where tags have been added to or removed from DNA after chemotherapy. These changes were related to our ability to sense and detect smells. The study by A/Prof Mikael Hartman and team was confirmed with a larger group of treated and untreated patients. The findings suggest that chemotherapy might affect our sense of smell by modifying the behavior of specific genes. This discovery helps us understand the biological underpinnings of why loss of smell is a common side effect associated with this cancer treatment.

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Histone Methyltransferase NSD2 Activates PKCα to Drive Metabolic Reprogramming and Lenalidomide Resistance in Multiple Myeloma

(Cancer Research, Chong PSY et. al.)

Multiple myeloma cells adapt to the harsh bone marrow environment by changing their metabolism. This change affects how the cells use energy and involves a protein called NSD2. Another protein, $PKC\alpha$, controls this process, making the cells less responsive to certain drugs. This collaborative study by Prof Chng Wee Joo and team suggests that targeting the energy process influenced by NSD2 could be a potential treatment for this type of blood cancer, especially for patients resistant to certain drugs. Elevated levels of a substance called lactate in the blood could indicate this resistance.



Read More

Spatiotemporal genomic profiling of intestinal metaplasia reveals clonal dynamics of gastric cancer progression (Cancer Cell, Huang K.K. *et. al.*)



Intestinal metaplasia (IM), often symptomless, poses a six-fold increased risk of stomach cancer. In this cross-institutional study, co-led by N2CR member Prof Jimmy So, researchers have identified 26 IM driver genes pivotal in the transition to cancer. The findings, published in Cancer Cell, was the world's largest genomic survey of over 1,100 samples of IM. This significant discovery offers insight into the processes that control the transformation to stomach cancer, providing a crucial opportunity for early detection and focused prevention. **Read More**

Dynamic altruistic cooperation within breast tumors

(Molecular Cancer, Masroni, M.S.B., Lee, K.W., Lee, V.K.M.et. al.)

Social behaviors such as altruism, where one self-sacrifices for collective benefits, critically influence an organism's survival and responses to the environment. Such behaviors are widely exemplified in nature but have been underexplored in cancer cells which are conventionally seen as selfish competitive players. This multidisciplinary study by Dr Leong Sai Mun, Dr Muhammad Sufyan and team explores altruism and its mechanism in breast cancer cells', and its contribution to chemoresistance.



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Highlights of 2023

N2CP STAFF RETREAT

Our first staff retreat was a great hit with an afternoon of intellectually stimulating discussions! Hope you are all excited for the next one coming up on 8 March 2024!





Advancing early detection of stomach cancer through trailblazing research

Stomach cancer is usually known as as 'ticking time bomb' as symptoms customarily only detected when the cancer has advanced. N2CR member Prof Jimmy So was part of a team that helped uncover genetic factors that could lead to early cancer detection, especially for patients with intestinal metaplasia; whom have a high risk of developing stomach cancer. This revolutionary finding can also help in the development of mass screening tools for stomach cancer.

A/Prof Polly Chen is the RNA Research Ambassador 2023!

Learn more about A/Prof Chen and her career journey to becoming a respected voice in the field of RNA, being the only person from Singapore to be an RNA Research Ambassador 2023

Click the video to learn more about her research amibitions

POSTDOC & GRADUATE STUDENT CLUB

N2CR launches the Postdoc and Graduate Student Club!

First launched in 2023 with Dr Kong Li Ren, the Club invites young researchers to share more about their post graduate journeys with new postdocs and graduate students to let them know about the different career paths open to them post PhD. Feeling a little stuck in the rut? Head on over to the next session for some much-needed inspiration.



Research highlights of 2023



"Ketogenic diet promotes tumor ferroptosis but induces relative corticosterone deficiency that accelerates cachexia" – Cell Metabolism, Volume 35, Issue 7, 11 July 2023

This study shows how a ketogenic diet can slow down cancer growth but may cause weight loss (cachexia). Using medication (dexamethasone) alongside the diet helps reduce side effects and improves survival.

Professor Ashok Venkitaraman

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"Berberine: Fighting Breast Cancer's Spread through Gut Bacteria & Natural Chemicals" – Pharmacological Research, Volume 193, July 2023

This study investigated the therapeutic possibilities of berberine on breast cancer cells, such as the ability to effectively hinder the growth and metastasis of breast cancer cells in an environment with low oxygen levels.

Associate Professor Gautam Sethi

Assistant Professor Derrick Ong

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"CAMK2D serves as a molecular scaffold for RNF8-MAD2 complex to induce mitotic checkpoint in glioma" – Cell Death and Differentiation, Volume 30, Aug 2023

The study explains how a group of proteins (RNF8, MAD2, and CAMK2D) work together to regulate cell division, particularly in brain cells (gliomas), and suggests that targeting these proteins could be a potential treatment for gliomas.

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"Indirect Treatment Comparison of First-Line CDK4/6-Inhibitors in Post-Menopausal Patients with HR+/HER2- Metastatic Breast Cancer " – Cancers, Volume 18, 14 Sept 2023

This study showcased that three different drugs for advanced breast cancer in postmenopausal women were found equally effective in improving survival, giving patients multiple treatment options.

Dr Joline Lim & Assistant Professor Raghav Sundar

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Upcoming Events

Sign-ups for CanCycle cyclethon and fundraising are still open until 29 Feb 2024! Keep healthy by cycling to raise funds for better and more targeted cancer treatments.

Sign up here!

WS Centre for Cancer Research Cong Loo Lin School of Medicine Early Cancer Intervention from Laboratory Discoveries to the Community

13 - 14 May 2024 | NUS MD6 Lecture Theatre 35 Guest of Honour : Professor Tan Chorh Chuan

N2CR INSIGHTS

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