JOINT NEWS RELEASE

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NTU Singapore's TARIPH Centre leads multi-institution research programme with first national research grant for lung health

The Academic Respiratory Initiative for Pulmonary Health (TARIPH) Centre, a national research platform led by **Nanyang Technological University, Singapore's (NTU Singapore) Lee Kong Chian School of Medicine (LKCMedicine)**, will lead a multi-institutional research programme after being awarded Singapore's first national research grant for respiratory health.

Under the **$10 million Open Fund-Large Collaborative Grant** (OF-LCG) supported by the National Research Foundation, Singapore (NRF) and administered by the Singapore Ministry of Health (MOH) through the National Medical Research Council Office, MOH Holdings Pte Ltd, the TARIPH Centre will collaborate with partners to conduct patient-centric translational research on respiratory health.

The NTU-led research programme brings together researchers from nine organisations, which includes all public healthcare clusters, medical schools and public agencies, alongside industry and international partners, to conduct Asian-centric lung health research across five different and integrated themes.

The team will focus on factors unique to Asia to provide a clearer understanding of the health, environmental, social and cultural needs of patients with lung diseases, allowing for personalised and precision-tailored treatments for Asian patients with chronic lung disease. This will ensure the development of effective national and

regional strategies to improve lung health, especially for persons living with chronic lung conditions like asthma and Chronic Obstructive Pulmonary Disease (COPD) in an era of climate change and an ageing population.

Researchers involved in this interdisciplinary collaborative initiative hail from NTU, Singapore General Hospital (SGH), National University Hospital (NUH), Tan Tock Seng Hospital (TTSH), National University of Singapore's (NUS) Faculty of Science, National Healthcare Group Polyclinics (NHG Polyclinics), Alexandra Hospital, NUS Yong Loo Lin School of Medicine, and A*STAR Institute for Human Development and Potential (A*STAR IHDP), allowing for a comprehensive and integrated programme that taps the full spectrum of research capabilities in Singapore, ranging from academic research to clinical innovation.

Professor Joseph Sung, NTU Senior Vice President (Health and Life Sciences) and Dean of NTU LKCMedicine, said: "The TARIPH Centre and its partners being awarded the Open Fund-Large Collaborative Grant signals the urgent need to bolster our national strategy to the increasing prevalence of lung conditions in Singapore and the emerging health effects of climate change. With the Centre able to leverage its successful collaborative framework that has been in place since 2018 and the research programme's aim to address crucial knowledge gaps in understanding respiratory health and treatment in Asians, this multi-institutional programme will position Singapore as a key respiratory research hub in Asia."

Associate Professor Sanjay Haresh Chotirmall, Vice-Dean of Research, NTU LKCMedicine, TARIPH OF-LCG Corresponding Principal Investigator (PI) and Theme 3 PI, said: "Existing knowledge on respiratory diseases is largely based on non-Asian populations, including most guidelines for diagnosis and management. Only a limited number of clinical studies focus solely on Asian patients. This leaves us with many unanswered questions: Is the disease the same in Asians? Do Asians respond the same way to medications? What are the effects of ethnicity, diet, and climate? Through this national research programme, TARIPH and its partners aim to close the significant knowledge gap in understanding respiratory disease in Asia."

Wide-ranging lung health studies across five key themes

The TARIPH research programme will run for five years until 2029 and **covers five themes.**

It examines the rise in chronic lung diseases in Singapore, such as asthma and COPD; best practices for post-intensive care patients; the emerging respiratory health effects of climate change; the impact of climate and environmental factors on the development of respiratory allergies and diseases in Singapore; and the establishment of a national repository of cellular airway models for research on targeted and personalised treatment for lung diseases.

Led by Assistant Professor Tiew Pei Yee and Associate Professor Mariko Koh from SGH, Associate Professor Sanjay Chotirmall from NTU LKCMedicine and TTSH, and Associate Professor Tang Wern Ee from NHG Polyclinics and NTU LKCMedicine, the **first theme aims to increase awareness of chronic lung diseases with early detection, and strengthen diagnostic and management tools for asthma in primary care.**

The researchers will embark on three complementary studies. The first study recruits a multi-ethnic group of early COPD patients in Singapore to examine how the disease starts and develops in Asians and differences between ethnic groups (i.e. Chinese, Malay and Indian). This will allow healthcare providers to better understand the disease and its treatment, improving the healthcare outcomes for Asian patient populations through identifying the disease early and intervening appropriately.

The second study explores the use of incorporating a simple blood test in the management of asthma in primary care, compared to the current practice of adjusting medications mainly based on patients' self-reports of their symptoms. Lastly, the researchers will also examine the side effects of long-term oral steroid therapy used in the management of severe asthma for some patients, as complications appear to be more common in Asians compared to non-Asians.

Assistant Professor Tiew Pei Yee, Senior Consultant, Department of Respiratory & Critical Care Medicine, SGH and Theme 1 PI, said: "Our research in this theme represents a significant step forward in addressing chronic lung diseases in Singapore's multi-ethnic population. Looking at the condition comprehensively from onset to development and long-term management will provide valuable insights to guide patient care and inform public health strategies."

The **second theme examines the impact of an Intensive Care Unit (ICU) stay on patients with respiratory diseases**. Led by Dr Matthew Cove from NUH and Adjunct Professor Jason Phua from Alexandra Hospital, this theme's focus is post-intensive care syndrome (PICS), where patients suffer from chronic long-term complications after discharge, such as difficulty in walking, cognitive issues, reduced physical function and mental health problems.

By better understanding the impact on health and quality of life after discharge, the theme seeks to identify and predict PICS development, allowing for healthcare providers to better manage the health and plan the care of patients after ICU stays and discharge from the hospital.

Dr Matthew Cove, Senior Consultant, Division of Respiratory & Critical Care Medicine, Department of Medicine, NUH and Theme 2 PI, said: "Respiratory failure is a leading cause of ICU admissions. Thankfully, advancements in critical care have significantly improved survival rates. However, surviving ICU is just the beginning for many patients. Over the past two decades, we have gained a better understanding of the significant

challenges faced by survivors, which can impact their quality of life. This grant will enable us to explore, in greater depth, the underlying factors and mechanisms behind these issues on a national scale. In the 21st century, survival alone is not enough — we want our patients to survive and thrive."

The **third theme aims to develop a national repository of lungs-in-a-dish cell models that can be used for lung disease research, drug screening, and testing of new treatments**.

The researchers, NTU Associate Professor Sanjay Chotirmall, Associate Professor Thai Tran and Professor Wang De Yun from NUS Medicine, will use advanced techniques to create organoids – tiny lung models grown in the lab that mimic how lungs function in real life – and Precision Cut Lung Slices (PCLS), which are thin pieces of human lung tissue kept alive in the lab, from Singaporean patient samples.

These cellular models will be made available nationally and internationally as a readily accessible Asian-centric bioresource, which can be quicky deployed in the laboratory to test against any new 'Disease X' in the event of a new potential pandemic.

The **fourth theme develops, models and tests the implementation of a nation-wide forecasting tool for asthma and COPD based on weather changes that may trigger patients with respiratory diseases**. This includes, for example, periods of poor air quality due to haze, or extreme rain and/or flooding, as climate change contributes to more extreme weather patterns.

Patients will be alerted to these weather changes through SMS, allowing them to make informed decisions to stay indoors, avoid exposure and manage the health risks caused by environmental and climate change. This in turn reduces the chances of triggering allergic reactions or respiratory attacks and infections.

The theme, led by Adjunct Professor John Abisheganaden and Associate Professor Angela Chow from TTSH, along with Associate Professor Steve Yim from NTU Asian School of the Environment and LKCMedicine, and Assistant Professor Lim Jue Tao from NTU LKCMedicine, aims to prevent acute deterioration events or exacerbations of respiratory disease and reduce emergency admissions triggered by climatic change.

Adjunct Professor John Abisheganaden, Senior Consultant, Department of Respiratory & Critical Care Medicine, TTSH and Theme 4 PI, said: "We will develop and pilot a novel forecasting tool, tailored for our local population, to testbed a digital health solution in the era of dynamic climate change. Specifically, with the use of big data, we will develop and implement a health-forecasting tool for predicting the probability of exacerbations of asthma and COPD, integrating relevant environmental and climatic triggers to predict for a respiratory health alert system. With the tool and alert system, patients and their caregivers can take necessary proactive measures to reduce exposure, thereby reducing unnecessary hospital utilisation."

The **fifth theme, which examines the role of environmental and climate change on respiratory diseases,** is led by NUS Associate Professor Chew Fook Tim and Dr Evelyn Loo Xiu Ling from A*STAR IHDP.

Allergic diseases, including asthma, are driven by a combination of genetic and environmental factors. The researchers will tap on three established local cohort studies and databases to study how climate and environmental factors can influence the development of respiratory allergies and diseases in Singaporeans throughout their life trajectory, from as early in their mother's womb.

They will also investigate how Asian diets and lifestyle habits play a part in the development of allergies.

Associate Professor Chew Fook Tim from the Department of Biological Sciences at the NUS Faculty of Science and Theme 5 PI said: "We have clear evidence that allergic diseases are driven by a combination of genetic and environmental factors. We have found that living in tropical climates can contribute to respiratory disease-related symptoms as compared to non-tropical climates. We aim to assess the role of gene-environment interactions with focus on environmental exposures such as allergens and the microbiome, as well as dietary and lifestyle factors that determine sensitisation, disease development and exacerbation."

More information on the studies in each of the five themes can be found in the **Annex**.

Patient-centric research designed with and for patients as key partners

The TARIPH research programme has taken a fresh approach in embedding patients as key partners to better understand their needs that require research to address.

It will engage patient partners through the TARIPH Lung Patient Network, which was launched in September 2023 as Singapore's first respiratory patient panel for medical research. This **patient-researcher collaboration** sees patients as partners and not mere participants, where patient views and voices, through lived experience, are actively sought out in the design, execution and reporting of research.

For example, under Theme 1, patients living with chronic lung conditions such as asthma and COPD will be involved in the study's design and execution, sharing their experiences to help researchers understand their challenges and improve recruitment. Some may act as advisors, ensuring the research stays focused on real-world problems and leading to better care for patients like them with its findings.

Researchers in Theme 2 will follow ICU patients up to six months after discharge to observe their recovery. ICU survivors and their caregivers will be invited to assist with designing the study to ensure it captures the most meaningful recovery outcomes for

patients.

Under Theme 4, patients will be directly involved in co-developing and testing the forecasting tool to ensure the alerts are clear, useful, and easy to follow. The messaging will be co-designed by patients for patients and their feedback will be collated through patient focus groups, which will address how the messaging fits into their daily routines and the tool's design and function.

The lived experiences and insights of the patient partners are a fresh, novel and crucial resource for the TARIPH research programme as it enables the research team to understand what matters most to patients and caregivers, and importantly contextualise this to address the unique needs of Singaporeans living with chronic lung disease.

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About Nanyang Technological University, Singapore

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 35,000 undergraduate and postgraduate students in the Business, Computing & Data Science, Engineering, Humanities, Arts, & Social Sciences, Medicine, Science, and Graduate colleges.

NTU is also home to world-renowned autonomous institutes – the National Institute of Education, S Rajaratnam School of International Studies and Singapore Centre for Environmental Life Sciences Engineering – and various leading research centres such as the Earth Observatory of Singapore, Nanyang Environment & Water Research Institute and Energy Research Institute @ NTU (ERI@N).

Under the NTU Smart Campus vision, the University harnesses the power of digital technology and tech-enabled solutions to support better learning and living experiences, the discovery of new knowledge, and the sustainability of resources.

Ranked amongst the world's top universities, the University's main campus is also frequently listed among the world's most beautiful. Known for its sustainability, NTU has achieved 100% Green Mark Platinum certification for all its eligible building projects. Apart from its main campus, NTU also has a medical campus in Novena, Singapore's healthcare district.

For more information, visit www.ntu.edu.sg

About National University of Singapore (NUS)

The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 16 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established more than 20 NUS Overseas Colleges entrepreneurial hubs around the world.

Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in

our faculties, research centres of excellence, corporate labs and more than 30 university-level research institutes focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

For more information on NUS, please visit nus.edu.sg.

About Singapore General Hospital (SGH)

Singapore General Hospital, established in 1821, is the largest tertiary hospital in Singapore and ranked among the world's best. It provides the most comprehensive patient-centred care with over 50 clinical specialties on its campus. As an Academic Medical Centre, it takes pride in training healthcare professionals and conducting cutting edge research to meet evolving needs of the nation as well as the region. Driven by a strong sense of purpose, SGH is committed to give of its best to heal and bring hope, as it has for over 200 years.

For more information, please visit www.sgh.com.sg

About the National University Hospital (NUH)

The National University Hospital (NUH) is Singapore's leading university hospital. While the hospital at Kent Ridge first received its patients on 24 June 1985, our legacy started from 1905, the date of the founding of what is today the NUS Yong Loo Lin School of Medicine. NUH is the principal teaching hospital of the medical school.

Our unique identity as a university hospital is a key attraction for healthcare professionals who aspire to do more than practise tertiary medical care. We offer an environment where research and teaching are an integral part of medicine, and continue to shape medicine and transform care for the community we care for.

We are an academic medical centre with over 1,200 beds, serving more than one million patients a year with over 50 medical, surgical and dental specialties. NUH is the only public and not-for-profit hospital in Singapore to provide trusted care for adults, women and children under one roof, including the only paediatric kidney and liver transplant programme in the country.

The NUH is a key member of the National University Health System (NUHS), one of three public healthcare clusters in Singapore.

About Tan Tock Seng Hospital (TTSH)

Tan Tock Seng Hospital (TTSH) is one of the longest serving and largest multi-disciplinary hospitals in Singapore. Recognised as the people's hospital, the 10,000-strong institution operates over 2,000 beds and covers more than 60 clinical disciplines. It anchors the 17-hectare HealthCity Novena, a strategic development to create an integrated community of healthcare, medical education and translational research.

Together with its centres of excellence – National Centre for Infectious Diseases (NCID), Institute for Geriatrics & Active Ageing (IGA), NHG Eye Institute (NHGEI), Trauma Centre and the TTSH Rehabilitation Centre – this leading tertiary institution is a pioneer in care, innovation and workforce transformation.

The flagship hospital of the National Healthcare Group, TTSH plays a pivotal role in creating new models of care and adding years of healthy life to the people of Singapore.

About the National Medical Research Council (NMRC)

The NMRC was established in 1994 to oversee research funding from the Ministry of Health and support the development and advancement of biomedical research in Singapore, particularly in the public healthcare clusters and medical schools. NMRC engages in research strategy and planning, provides funding to support competitive research grants and core research enablers, and is responsible for the development of clinician scientists through awards and fellowships. The council's work is supported by the NMRC Office which is part of MOH Holdings Pte Ltd. Through its management of the various funding initiatives, NMRC promotes healthcare research in Singapore, for better health and economic outcomes.

ANNEX

Details of research themes under the TARIPH Research Programme

Theme and Principal Investigators	Study details
Multi-ethnic Endo-Phenotyping of Asthma and COPD (MEPAC) Principal investigators: Assistant Professor Tiew Pei Yee (SGH) Associate Professor Sanjay Haresh Chotirmall (NTU LKCMedicine and TTSH) Associate Professor Mariko Koh Siyue (SGH) Associate Professor Tang Wern Ee (NHG Polyclinics and NTU LKCMedicine) NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE / LEE KONG CHIAN SCHOOL OF MEDICINE Singapore General Hospital SingHealth National Healthcare Group Adding years of healthy life / National Healthcare Group POLYCLINICS	The Multi-ethnic Endo-Phenotyping of Asthma and COPD (MEPAC) theme aims to increase awareness of chronic lung diseases with early detection, strengthen diagnostic and management tools for asthma in primary care. It also addresses complex issues like the side effects of steroid use. It comprises three studies. The first aims to recruit a multi-ethnic group of early Chronic Obstructive Pulmonary Disease (COPD) patients in Singapore to examine how the disease starts and develops. As the onset and progression of COPD can differ among Asians and between different ethnic groups, this study will better understand the disease and its treatment in the Asian context. This can then improve the healthcare outcomes of Asian patient populations through identifying the disease early, intervening and potentially stopping the disease from progressing. The second study explores the use of a simple blood test to guide treatment of asthma in Asian patients in the primary care setting. It will perform a randomised clinical trial in the primary care setting to assess if use of the blood test can help primary care doctors better manage patients with asthma, and aid in asthma medication dose adjustments in primary care. The third study seeks to gain insights about how different ethnic groups in the severe asthma patient population are uniquely affected by the medical complications from

	long-term oral steroid therapy used in the management of severe asthma. Many patients still rely on the oral steroids to manage their disease as alternative treatment methods are currently expensive and, in many cases, inaccessible to most patients. However, oral steroids can lead to side effects like diabetes, heart disease, and weakened bones (osteoporosis). These complications appear to be more common in Asians compared to non-Asians and differ in occurrence and severity between the ethnicities suggesting that a tailored approach to prevention is needed. Using local and international data from the Singapore Severe Asthma Registry (SSAR) and the International Severe Asthma Registry (ISAR) in which Singapore participates, the study aims to create a risk prediction model unique to Singapore's main ethnic groups (Chinese, Malay, and Indian) to help doctors assess the potential complications for their patients, before and during therapy, thus enabling them to better manage the long-term health of the patients and prevent such side-effects.
Burden & biology of Post-Intensive Care Syndrome (2B-PICS) Principal investigators: Dr Matthew Cove (NUH) Adjunct Professor Jason Phua (AH)  	The two studies under this theme aim to better understand the impact of an ICU stay on a patient, focused on the post-discharge period when the patient has returned home. The impact on health and quality of life after discharge has not been extensively studied. Patients with severe respiratory conditions often suffer from chronic long-term complications after discharge, known as post-intensive care syndrome (PICS), which includes manifestations such as difficulty in walking, cognitive issues, reduced physical function and mental health problems.

Alexandra Hospital	These issues severely impact one's daily life and quality of life, and less than half of the patients after an ICU stay actually return to work within a year. The first study is an expansion of the existing National Intensive Care Unit Repository (NICUR), an initiative funded by the Ministry of Health (MOH) that collects ICU data on patients admitted to Singapore's public hospitals. Data collection is currently performed for only three months each year. The expansion will include data collection all year round and an additional assessment of patients' quality of life after ICU discharge to help identify patients at risk of developing PICS. The second study involves a detailed characterisation of immunological markers including cell types, inflammation and associated responses to identify objective blood markers that can predict the development and severity of PICS at the individual patient level, thereby guiding early identification of those most at-risk and improving their management. The research team will use the findings to work with Singapore's growing medtech innovation and research ecosystem to co-develop products that monitor and support post-ICU care, PICS management and outpatient rehabilitation.
Cellular Models of respiratory disease for Asian Phenotyping (CEMAP) Principal investigators: Associate Professor Sanjay Haresh Chotirmall (NTU LKCMedicine)	In collaboration with MOH's National Research Foundation, Singapore -funded Programme for Research in Epidemic Preparedness and REsponse (PREPARE), the studies in Theme 3 aim to develop various "lungs-in-a-dish" cell models to facilitate research on lung disease, drug screening and to allow assessment of novel treatments.

Associate Professor Thai Tran (NUS Medicine) Professor Wang De Yun (NUS Medicine)   	These models include organoids – tiny lung models grown in the lab which mimic how lungs function in real life – and Precision Cut Lung Slices (PCLS), which are thin pieces of human lung tissue kept alive in the lab for research use. This allows scientists to study how the lung works and test treatments in a way that mimics real-life conditions Researchers will focus on creating a comprehensive national repository of upper (nose) and lower (lung) airway models to facilitate research on targeted treatment for lung diseases in Asian populations and in preparation for any potential future disease outbreaks as described above. The repository will facilitate international collaborations and establish Singapore as a leading research hub for respiratory medicine with academic and industry partners.
Forecasting COPD and Asthma attendances using Large-scale time Series for patient and policy support (FOCALS) Principal investigators: Adjunct Professor John Abisheganaden (TTSH) Associate Professor Angela Chow (TTSH) Associate Professor Steve Yim Hung Lam (NTU Asian School of the Environment and LKCMedicine) Assistant Professor Lim Jue Tao (NTU LKCMedicine)	Climate change is an increasing global threat that is contributing to more adverse and extreme weather patterns. FOCALS aims to develop a nation-wide forecasting alert system that can inform and warn patients of potential weather and environmental factors which may pose a threat to their respiratory health. This includes, for example, periods of poor air quality due to haze, or extreme rain and/or flooding. The aim of the alert system is to predict and prevent asthma and COPD flare-ups due to adverse weather conditions, and reduce healthcare usage through prevention, thereby resulting in better patient outcomes and cost savings for both patients and hospitals. Patients will be alerted to these weather changes through SMS, allowing them to

  	make informed decisions to stay indoors, avoid exposure and manage the dynamic health risks based on environmental and climate change. This in turn reduces the chances of triggering allergic reactions or respiratory attacks and infections. The forecasting system will also help hospitals project and manage surges in demand for their emergency services, allowing them to plan and respond in a timely manner.
Climate change, Allergy, Pollution, and the Environment (CAPE) Principal investigators: Associate Professor Chew Fook Tim (NUS) Dr Evelyn Loo Xiu Ling (A*STAR IHDP)  	Allergic diseases, including asthma, are driven by a combination of genetic and environmental factors. This theme examines three existing local cohort studies and databases to study how climate and environmental factors can influence the development of respiratory allergies and diseases in Singaporeans throughout their life trajectory, from as early as they were in the mother's womb. The studies are: Growing Up in Singapore Towards Healthy Outcomes (GUSTO), Singapore Preconception Study of Long-Term Maternal and Child Outcomes (S-PRESTO) and the Singapore-Malaysia Cross Sectional Genetic Epidemiology Study (SMCGES). Researchers will also investigate how Asian diets and lifestyle habits play a part in the development of allergies. The results will be used to suggest preventive measures or early intervention to be put in place at the individual, system, hospital and national levels, and will include public policy on environmental risk, surveillance, construction, and health protective measures under the national HealthierSG initiative.

About TARIPH Lung Patient Network

The TARIPH Lung Patient Network is part of a larger LKCMedicine-wide network of patients and caregivers known as OPEN Voices.

Launched on 20 September 2023, the TARIPH Lung Patient Network represents the first patient panel focused on developing respiratory research by patients for patients in Singapore. It serves as a platform for individuals living with chronic lung diseases and their caregivers to be empowered in becoming active research partners going beyond only being involved as research participants. They do this by participating in study design, execution, interpretation of results and communication of its findings.

The patient partners have been involved in a study exploring lived experience and perception of clinical research in people living with lung conditions, by providing inputs on the survey design and the interpretation of study findings. The patients are equal co-authors on a research manuscript describing the study findings that will shortly be submitted to a medical journal for publication.

The Network currently has 13 patient partners.