

Singapore's respiratory health gets a boost with \$10 million research grant

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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 personalized 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 aging 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. 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 multiinstitutional programme will position Singapore as a key respiratory research hub in Asia."

Professor Joseph Sung, NTU Senior Vice President (Health and Life Sciences) and Dean of NTU LKCMedicine

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 <u>diagnosis</u> 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 utilization." 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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