

JOINT NEWS RELEASE

Singapore, 15 September 2022

International study led by Singapore scientists discovers bacteria previously thought harmless can worsen existing lung disease

A team of international scientists led by **Nanyang Technological University, Singapore (NTU Singapore)** has discovered that *Neisseria* – a genus of bacteria that lives in the human body – is not as harmless as previously thought, and can cause infections in patients with bronchiectasis, asthma, and chronic obstructive pulmonary disease (COPD).

In a landmark study, published today in the scientific journal *Cell Host & Microbe*, the team showed conclusive evidence that *Neisseria* species can cause disease in the lung and are linked to worsening bronchiectasis (a type of lung disease) in patients.

Bronchiectasis is a long-term condition where the airways of the lungs become abnormally enlarged for unknown reasons in up to 50 per cent of Singaporean patients. The disease is up to four times more prevalent among Asians as compared to their Western counterparts and can also occur following recovery from tuberculosis.¹ In Singapore, research at Tan Tock Seng Hospital described 420 incident hospitalised bronchiectasis patients in 2017.² The incidence rate is 10.6 per 100,000 and increases strongly with age.

Despite its prevalence among older people, no obvious cause is found in most cases of bronchiectasis and the condition tends to arise spontaneously and without warning.³

To unravel the puzzle of why bronchiectasis worsens at a significantly greater rate among older Asian patients, the international team – spanning researchers and hospitals in Singapore, Malaysia, China, Australia, and the UK (see *Annex*) – led by **NTU's LKCMedicine Associate Professor Sanjay Chotirmall, Provost's Chair in Molecular Medicine**, matched disease and infection data from 225 patients with bronchiectasis of Asian (Singapore and Malaysia) origin to those from bronchiectasis patients in Europe.

¹ [Trends in Bronchiectasis Among Medicare Beneficiaries in the United States, 2000 to 2007](#)

² [Epidemiology and economic burden of bronchiectasis requiring hospitalisation in Singapore](#)

³ [Geographic variation in the aetiology, epidemiology, and microbiology of bronchiectasis](#)

Neisseria: not so harmless after all

While *Neisseria* species are well known to cause meningitis and gonorrhoea, they are not known to infect lungs. Through detailed identification and meticulous characterisation, the research team found that *Neisseria* dominated the microbiome of Asian patients with worsening bronchiectasis.

Specifically, bronchiectasis patients with predominant amounts of a subgroup of *Neisseria* called ***Neisseria subflava* (*N. subflava*)**, experienced more severe disease and repeated infections (exacerbations) when compared to patients with bronchiectasis without such high amounts of *Neisseria*.

Upon further investigation using experimental cell and animal models, the research team confirmed that ***N. subflava*** causes cell disruption, resulting in inflammation and immune dysfunction in bronchiectasis patients with this bacterium.

Prior to this discovery, *Neisseria* was not considered to be a cause of lung infection or severe disease in bronchiectasis patients.

Lead investigator Assoc Prof Chotirmall said, “Our findings have established, for the first time, that poorer clinical outcomes such as greater disease severity, poorer lung function and high repeated infection rates among bronchiectasis patients are closely associated to the bacteria *Neisseria* and that this finding is especially important for Asian patients.”

“This discovery is significant because it can change how we treat our bronchiectasis patients with this bacterium. Doctors will now need to think about *Neisseria* as a potential ‘culprit’ in patients who are worsening despite treatment, and to conduct tests to identify those who may be harbouring this type of bacteria in their lungs. We hope that early identification will lead to personalised therapy, and consequently, better disease outcomes for Asian patients with this devastating disease,” said **Assoc Prof Chotirmall**, who is also Assistant Dean (Faculty Affairs) at LKCMedicine.

This study reflects NTU’s efforts under **NTU2025**, the University’s five-year strategic plan that addresses humanity’s grand challenges such as human health. Conducted by international researchers from across various disciplines, the study also highlights NTU’s strength and focus on interdisciplinary research.

Broader relevance of *Neisseria*

Aside from linking *Neisseria* and severe bronchiectasis, the NTU-led research team also detected the presence of the same bacteria in other more common chronic respiratory conditions such as severe asthma and Chronic Obstructive Pulmonary

Disease (COPD) – a condition that causes airflow blockage and breathing-related problems.

Using next-generation sequencing technologies, the team also sought to investigate where this bacterium may come from and sampled the homes of bronchiectasis patients with high amounts of *Neisseria* in their lungs. The researchers found the presence of the bacteria in the home environment, suggesting that the indoor living space and potentially the tropical climate may favour the presence of this bacteria in the Asian setting.

What is *Neisseria*?

The *Neisseria* bacteria species have been commonly identified as the cause of sexually transmitted infection like gonorrhoea but also critically meningitis - an inflammation of the fluid and membranes surrounding the brain and spinal cord. Its sub-species *N. subflava*, however, is known to be found in the oral mucosa, throat, and upper airway of humans previously without any known link to lung infections.

This family of bacteria has always been thought of as harmless to humans, and infections caused by them have not been described – until now.

Co-author, Professor Wang De Yun from the Department of Otolaryngology at the Yong Loo Lin School of Medicine, National University of Singapore, said, “It is encouraging to see that we have made headway in identifying the *Neisseria* bacteria species as the cause of worsening bronchiectasis, the unlikely culprit that was originally not considered to be a threat. This comes as a strong reminder that we should not be too complacent when it comes to doing research and exercise more proactiveness in exploring various possibilities, as every seemingly innocent element could be a source of threat to our bodies and overall health.”

Co-author Andrew Tan, Associate Professor of Metabolic Disorders from LKCMedicine, said, “The reverse translational approach adopted in this work was crucial to our success. Starting from the ‘bedside’ where we studied real-life patient experiences, we then worked backwards to uncover the biological process of the bacteria. Thanks to the interdisciplinary nature of the study, the team was able to interact with members from different research disciplines, offering an enjoyable experience while gaining unique insights into the disease.”

The researchers are now looking to conduct further studies and clinical trials of *Neisseria* eradication from the microbiome through the newly launched **LKCMedicine Centre for Microbiome Medicine**, which is seeking evaluate the benefits of targeting and treating *Neisseria* with antibiotics at first detection, with the hope that this will lead to better clinical outcomes for patients with chronic respiratory conditions.

Notes to Editor:

Paper titled "*Neisseria species as pathobionts in bronchiectasis*", published in Cell Host & Microbe, September 14, 2022. DOI: <https://doi.org/10.1016/j.chom.2022.08.005>

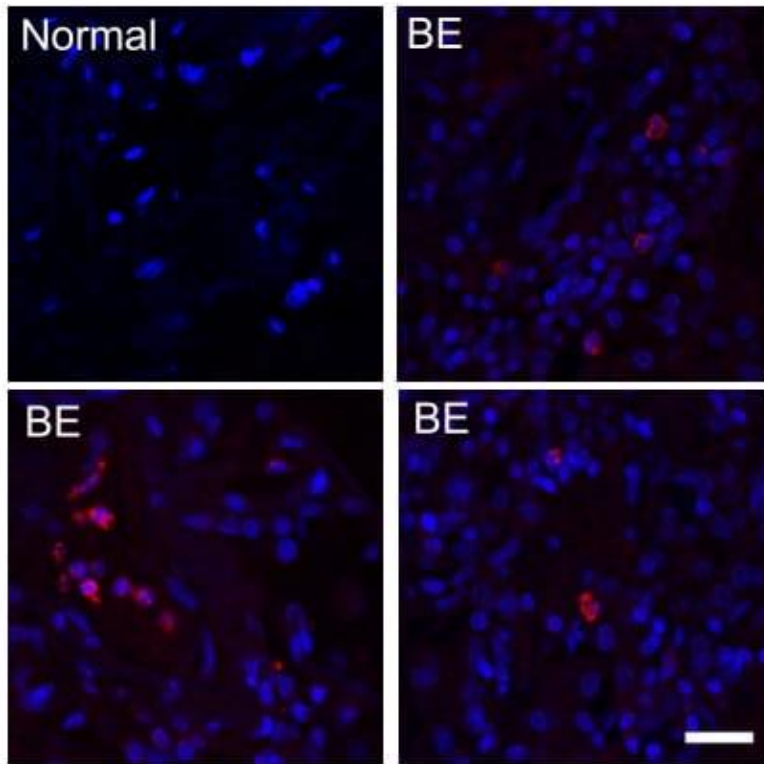


Image: Pictured is a detection of *Neisseria* (*N. subflava*) in lung tissue from patients with bronchiectasis. Shown in red is the *N. subflava* detection and shown in blue is the airway cell nuclei. *Credit: Cell Host & Microbe*

END

Media contact:

Ms Junn Loh
Manager, Media Relations
Corporate Communications Office
Nanyang Technological University, Singapore
Email: junn@ntu.edu.sg

Ms Amanda Yap
Assistant Manager, NUS Medicine Communications
Dean's Office, Yong Loo Lin School of Medicine
National University of Singapore
Email: medajy@nus.edu.sg

About Nanyang Technological University, Singapore

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 33,000 undergraduate and postgraduate students in the Engineering, Business, Science, Medicine, Humanities, Arts, & Social Sciences, and Graduate colleges.

NTU is also home to world-renowned autonomous institutes – the National Institute of Education, S Rajaratnam School of International Studies, Earth Observatory of Singapore, and Singapore Centre for Environmental Life Sciences Engineering – and various leading research centres such as the Nanyang Environment & Water Research Institute (NEWRI) 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, over 95% of its building projects are certified Green Mark Platinum. 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

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 our NUS Overseas Colleges programme in more than 15 cities 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, 30 university-level research institutes, research centres of excellence and corporate labs 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 www.nus.edu.sg.

Annex

List of collaborating institutions:

- Department of Pharmacology, School of Medicine, Southern University of Science and Technology, Shenzhen, China
- Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, China
- Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
- Biochemical Genetics Laboratory, Department of Biochemistry, St. James's Hospital, Dublin, Ireland
- Clinical Biochemistry Unit, School of Medicine, Trinity College Dublin, Dublin, Ireland
- School of Civil and Environmental Engineering, Nanyang Technological University, Singapore
- College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, China
- University of Dundee, Ninewells Hospital, Medical School, Dundee, Scotland
- Department of Otolaryngology, Infectious Disease Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore
- Department of Respiratory and Critical Care Medicine, Singapore General Hospital, Singapore
- Department of Respiratory and Critical Care Medicine, Tan Tock Seng Hospital, Singapore
- Department of Respiratory and Critical Care Medicine, Changi General Hospital, Singapore
- Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia
- Department of Respiratory Medicine and Critical Care, Peking University Shenzhen Hospital, Shenzhen, China
- Priority Research Centre for Healthy Lungs, Hunter Medical Research Institute, School of Medicine and Public Health, University of Newcastle, NSW, Australia
- Department of Respiratory and Sleep Medicine, John Hunter Hospital, New Lambton Heights, NSW, Australia
- Woolcock Institute of Medical Research, University of Sydney, Australia

- School of Life Sciences, University of Technology Sydney, Australia
- Singapore Centre for Environmental Life Sciences Engineering (SCELSE), Nanyang Technological University, Singapore
- School of Biological Sciences, Nanyang Technological University, Singapore
- Department of Environmental Science and Engineering, Fudan University, Shanghai, China

###