PRESS RELEASE FOR IMMEDIATE RELEASE

Ageing, smoking, oral bacteria and genetic mutations linked to higher stomach cancer risk

- *Duke-NUS and NUHS scientists uncover a complex web of genetic, age-related and microbial factors that increase the risk of stomach cancer.*
- *Age-related blood cell mutations may trigger early changes in the stomach lining, offering new insights into how cancer risk builds over time and underscoring the importance of healthy ageing.*
- *Findings point to new ways to identify individuals at highest risk of developing stomach cancer, opening opportunities for targeted prevention and precise screening.*

SINGAPORE, 19 JANUARY 2026—Scientists at Duke-NUS Medical School and the National University Health System (NUHS), together with an international team of researchers, have uncovered a complex interplay of factors that increase the risk of developing stomach cancer (gastric cancer). These factors include genetic and age-related blood mutations, smoking and infection by oral bacteria. Published in *Cancer Discovery*, the findings provide new insight into the earliest biological changes that precede the development of gastric cancer and could offer more precise approaches for risk stratification and prevention.

Gastric cancer remains one of the world's deadliest cancers. It is the fifth most common cancer and the fourth leading cause of cancer-related deaths globally, accounting for 769,000 deaths in 2020[1]. In Singapore, it is among the top 10 causes of cancer-related deaths, claiming about 300 lives[2] each year.

Gastric cancer typically develops over many decades, beginning with chronic inflammation in the stomach lining. This can progress to intestinal metaplasia, a condition in which normal stomach cells gradually convert to cells resembling those usually found in the intestines. Over time, these changes may progress to more severe tissue damage and cancer. However, clinicians have limited ability to predict which individuals with intestinal metaplasia are most likely to progress to gastric cancer.

To address this gap, studies were conducted under the Singapore Gastric Cancer Consortium (SGCC), a multidisciplinary national research programme comprising clinicians and scientists from various academic medical centres, universities and research institutes working in gastric cancer research and management. The SGCC team, which included collaborators from the National University of Singapore Yong Loo Lin School of Medicine (NUS Medicine), the Nanyang Technological University's Lee Kong Chian School of Medicine and A*STAR, along with clinicians from SingHealth, NHG Health, Hong Kong, Japan, South Korea, Taiwan and the USA, analysed more than 1,500 intestinal metaplasia samples collected across six countries. This large, geographically diverse dataset enabled the team to compare genetic changes across populations with differing levels of gastric cancer risk.

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer 1261 Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers 1262 in 185 Countries. CA Cancer J Clin 2021;71(3):209-49 doi 10.3322/caac.21660.
[2] Singapore Medical Association - For Doctors, For Patients (sma.org.sg)

Using advanced genetic analyses, the researchers identified 47 significantly mutated genes in intestinal metaplasia cells. Mutations in one particular gene, *ARID1A,* were associated with increased risk of gastric cancer and poorer prognosis. The team also uncovered a distinct pattern of DNA damage, known as SBS17, which was absent in healthy stomach tissue but commonly found in intestinal metaplasia. SBS17 is linked to oxidative stress—a type of cellular damage caused by reactive molecules generated by abnormal metabolism. This damage can be worsened by exposure to tobacco smoking. This finding suggests that oxidative stress may play a critical role in the earliest stages of gastric cancer development.

In another exciting development, the team also discovered that pyrvinium, a drug currently used to treat parasites, had the ability to inhibit the growth of intestinal metaplasia cells. Building on this finding, clinical studies under the SGCC are being planned to explore therapeutic strategies for intestinal metaplasia.

Unexpectedly, the team also discovered that clonal hematopoiesis, a process in which blood stem cells acquire mutations and multiply—was also associated with increased susceptibility to gastric cancer. Since clonal hematopoiesis is known to occur in the elderly, these findings further explain why gastric cancer is often diagnosed in patients later in their life. Further analysis revealed that individuals with clonal hematopoiesis also carried higher levels of oral bacteria such as *Streptococcus* in their stomachs. Together, the "dual-impact" of weakened immunity caused by clonal hematopoiesis, along with increased bacterial levels, may fuel chronic inflammation and accelerate progression to gastric cancer.

Professor Patrick Tan, Dean at Duke-NUS Medical School and a senior author of the study, said:
"Gastric cancer is often called a *silent killer* because it takes hold quietly, long before symptoms appear. What our study shows is that risk does not come from one place — it builds over many years through a complex interplay between ageing, genetic changes, immune shifts and even the bacteria we carry. As Singapore is a rapidly ageing population, these findings improve our understanding of biological processes that happen when we age and will contribute towards the nation's quest to promote healthy longevity and resilience."

Professor Yeoh Khay Guan, Chief Executive, NUHS and co-senior author of the study, said:
"Our findings open the door to exploring new and more effective treatments such as eliminating specific bacteria, and therapies to inhibit or potentially reverse intestinal metaplasia. These findings also provide insights into which intestinal metaplasia patients are at greatest risk of developing gastric cancer. These can serve as valuable biomarkers to identify the most vulnerable long before the disease strikes, guiding more focused screening to identify those who require closer monitoring."

Professor Yeoh is also a Senior Consultant in the Division of Gastroenterology & Hepatology at the National University Hospital, and the Kishore Mahbubani Professor in Medicine and Health Policy, Department of Medicine, NUS Medicine.

This research was supported by the Singapore Ministry of Health through the National Medical Research Council (NMRC) Office, MOH Holdings Pte Ltd under the NMRC Singapore Translational Research Investigator Award (MOH-000967), and the National Research Foundation, Singapore (NRF) under the NMRC Open Fund – Large Collaborative Grant (MOH-000206) administered by the Singapore Ministry of Health through the NMRC Office, MOH Holdings Pte Ltd.

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About Duke-NUS Medical School

Duke-NUS is Singapore's flagship graduate entry medical school, established in 2005 with a strategic, government-led partnership between two world-class institutions: Duke University and the National University of Singapore (NUS). Through an innovative curriculum, students at Duke-NUS are nurtured to become multi-faceted 'Clinicians Plus' poised to steer the healthcare and biomedical ecosystem in Singapore and beyond. A leader in ground-breaking research and translational innovation, Duke-NUS has gained international renown through its five Signature Research Programmes and ten Centres. The enduring impact of its discoveries is amplified by its successful Academic Medicine partnership with Singapore Health Services (SingHealth), Singapore's largest healthcare group. This strategic alliance has led to the creation of 15 Academic Clinical Programmes, which harness multi-disciplinary research and education to transform medicine and improve lives.

For more information, please visit www.duke-nus.edu.sg

About the National University Health System

The National University Health System (NUHS) aims to transform how illness is prevented and managed by discovering causes of disease, development of more effective treatments through collaborative multidisciplinary research and clinical trials, and creation of better technologies and care delivery systems in partnership with others who share the same values and vision.

Institutions in the NUHS Group include the National University Hospital, Ng Teng Fong General Hospital, Jurong Community Hospital and Alexandra Hospital; three National Specialty Centres - National University Cancer Institute, Singapore (NCIS), National University Heart Centre, Singapore (NUHCS) and National University Centre for Oral Health, Singapore (NUCOHS); the National University Polyclinics (NUP); Jurong Medical Centre; and three NUS health sciences schools – NUS Yong Loo Lin School of Medicine (including the Alice Lee Centre for Nursing Studies), NUS Faculty of Dentistry and NUS Saw Swee Hock School of Public Health.

With member institutions under a common governance structure, NUHS creates synergies for the advancement of health by integrating patient care, health science education and biomedical research.

As a Regional Health System, NUHS works closely with health and social care partners across Singapore to develop and implement programmes that contribute to a healthy and engaged population in the Western part of Singapore.

For more information, please visit www.nuhs.edu.sg.

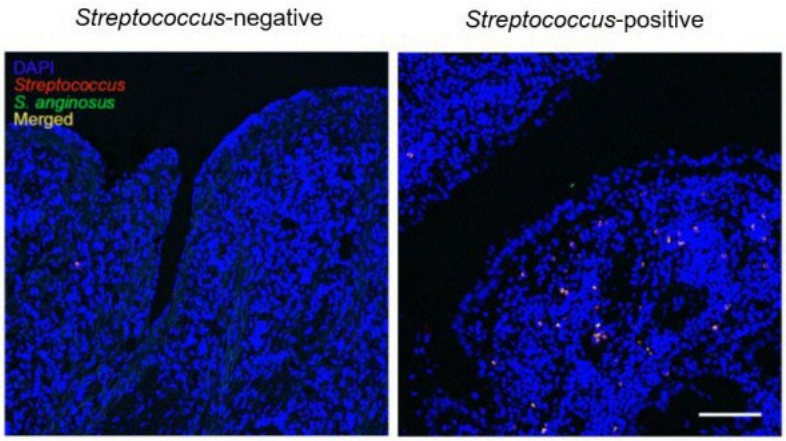
About the National Medical Research Council (NMRC)

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.

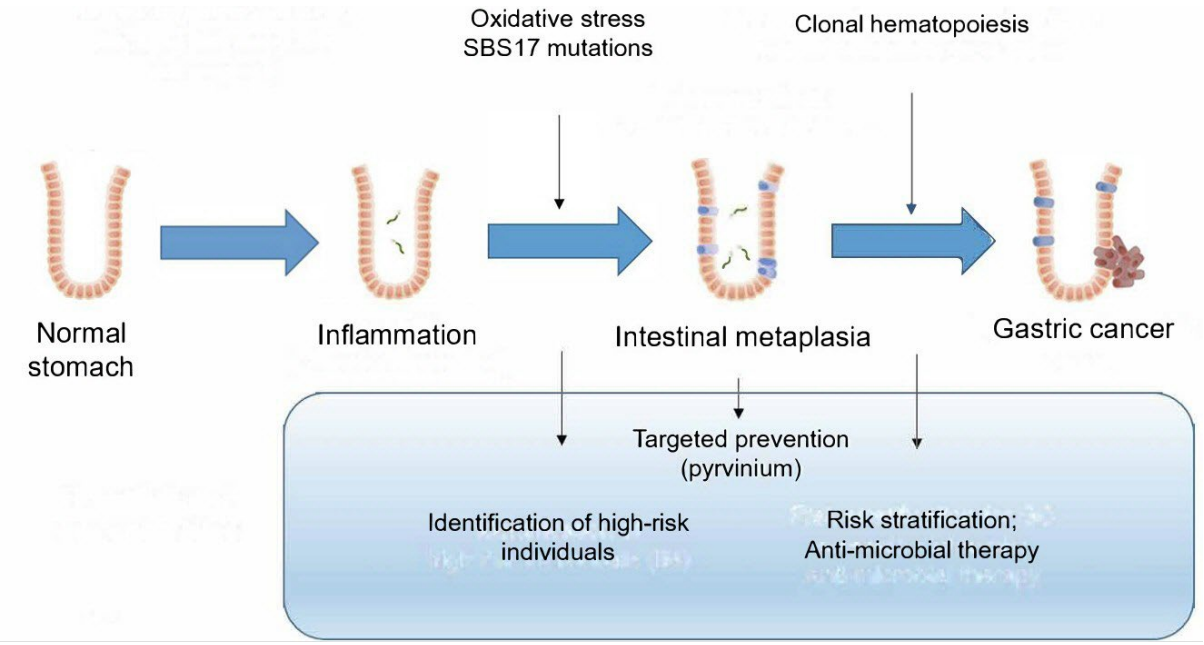
About the National Research Foundation (NRF)

The National Research Foundation, Singapore (NRF), set up on 1 January 2006, is a department within the Prime Minister's Office. The NRF sets the national direction for research and development (R&D) by developing policies, plans and strategies for research, innovation and enterprise. It also funds strategic initiatives and builds up R&D capabilities by nurturing research talent. Learn more about the NRF at www.nrf.gov.sg.

Annex B: Images



Caption: Detection of oral bacteria (red and green dots) in gastric cancer tissue. // Image credit: Lee Kong Chian School of Medicine



Caption: Factors contributing to gastric cancer and potential interventions. // Image credit: Duke-NUS Medical School

Annex C: Chinese Translations

Duke-NUS Medical School (Official name, for use on first reference)	杜克－新加坡国立大学医学院
Duke-NUS (abbreviated form)	杜克－国大医学院
National University Health System (NUHS)	国大医学组织
Singapore Gastric Cancer Consortium (SGCC)	新加坡胃癌研究团
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