Genomic profiling offers early clues to stomach cancer development

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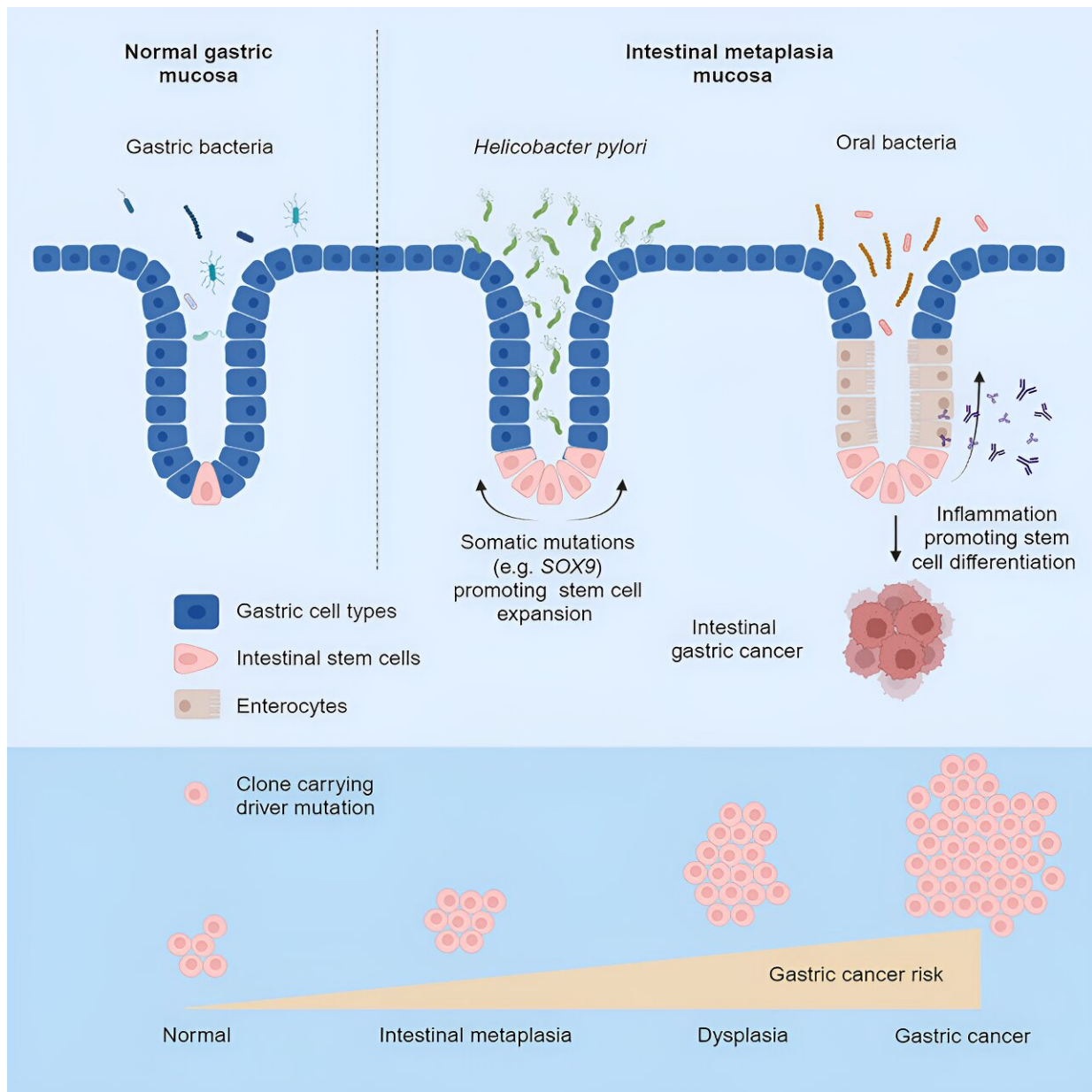
In a breakthrough study [published](#) in *Cancer Cell*, researchers have decoded critical genetic factors in intestinal metaplasia patients, shedding light on early signs and prevention strategies for stomach cancer—often a "ticking time bomb" as patients experience no or only mild symptoms in the early stages.

Intestinal metaplasia, which is a change in the cells of the mucous membrane lining the stomach that often stems from chronic gastritis and manifests with symptoms akin to acid reflux, is also a sinister link to [stomach cancer](#). Individuals afflicted with intestinal metaplasia cells face a six-fold increased risk of succumbing to this lethal [cancer](#).

In Singapore alone, stomach cancer ranks as the fourth leading cause of cancer deaths in men and the fifth among women, claiming 300 to 500 lives annually, largely due to late detection. Two thirds of stomach cancer patients are only diagnosed at an advanced stage.

Unveiling early indicators through collaborative breakthrough research

The [longitudinal study](#), which represents the world's largest genomic survey of patients with intestinal metaplasia, examines more than 1,100 tissue samples using powerful technologies such as single-cell RNA sequencing and spatial transcriptomics.

Based on this extensive survey, researchers identified 26 'driver genes' that play a pivotal role in the transition to stomach cancer. This landmark finding provides a glimpse into the mechanisms governing the

transformation and offers a critical window for early detection and targeted prevention.

"Advances in DNA sequencing have made it possible for us to uncover diverse cell populations within these stomach changes, hinting at their potential transformation into cancerous cells influenced by various factors. It's akin to understanding the ticking mechanism of a time bomb," explained Dr. Huang Kie Kyon, co-first author and Senior Research Fellow with the Cancer & Stem Cell Biology Program at Duke-NUS Medical School (Duke-NUS).

Professor Patrick Tan, Senior Vice-Dean for Research at Duke-NUS and a professor with the School's Cancer & Stem Cell Biology Program said, "The comprehensive dataset we've assembled provides unprecedented insights into the progression of cell changes in the stomach to cancer."

"By using both clinical information and genetic data from advanced molecular technologies, we can better predict which stomach conditions might turn into stomach cancer compared to using only clinical information. This can help in the development of new and more precise ways to prevent and stop stomach cancer."

Prof Tan is also a member of the Genome Institute of Singapore, Cancer Science Institute of Singapore, and Precision Health Research Singapore (PRECISE).

The multi-institutional effort by researchers from Duke-NUS, National University Hospital (NUH), National University of Singapore's Yong Loo Lin School of Medicine (NUS Medicine) and Seoul National University Hospital reflects the strengths of Singapore's multi-institutional cancer research ecosystem and its strong links with global partners.

This study was supported by the Singapore Gastric Cancer Consortium (SGCC), a national translational research group comprising clinicians and scientists working in stomach cancer research from academic medical centers, universities, hospitals and research institutes across Singapore. The published work is derived from the prospective Gastric Cancer Epidemiology Program cohort.

The study offers clues into whether intestinal metaplasia cells directly transform into stomach cancer. It was revealed that a subpopulation of intestinal stem-like cells in patients with intestinal metaplasia closely resembles early stomach cancer cells, pointing to a possible early origin and potential of its malignant future. This discovery highlights the importance of screening for intestinal metaplasia in managing stomach cancer risk.

Co-senior author Professor Jimmy So, Head & Senior Consultant, Division of General Surgery (Upper Gastrointestinal Surgery), NUH commented on the clinical implications saying, "This molecular roadmap of disease progression from intestinal metaplasia offers many translational opportunities."

"We can now explore more targeted surveillance for patients at highest risk, as well as anti-inflammatory or antibiotic agents to intercept premalignant clones before they evolve into cancer, potentially leading to improved patient outcomes through early detection." He is also a professor at the Department of Surgery, NUS Medicine.

More efficient and targeted preventive measures for populations

At the [population level](#), the findings hold promise for refining screening strategies and allocating resources more effectively to intercept the

development of gastric cancer in high-risk individuals, ultimately contributing to more efficient and targeted preventive measures. This is especially relevant in countries such as Singapore, where the incidence of stomach cancer is moderate compared to Japan and South Korea where stomach cancer incidence is high enough to warrant mass screening.

"Encouragingly, our results revealed that combining genomic data with clinical check-ups can make predictions about stomach cancer more accurate. This means we might use genetic tests, including simple and inexpensive blood tests, to identify people who are at a very high risk of getting stomach cancer," added Professor Khay Guan Yeoh, Lead Principal Investigator of the Singapore Gastric Cancer Consortium and Senior Consultant in the Division of Gastroenterology & Hepatology, National University Hospital.

"With this approach, we can divide people into groups based on their risk using either regular check-ups or these affordable blood tests. This helps to save resources by making sure those at the highest risk get the right tests and care they need." Prof Yeoh is also the Kishore Mahbubani Professor in Medicine and Health Policy, Department of Medicine, NUS Medicine.

Senior author Associate Professor Chung Hyunsoo from Seoul National University Hospital said, "This breakthrough may refine screening protocols, enabling early interventions for high-risk patients, while sparing others unnecessary procedures."

The project could not have been made possible without the contributions of researchers from Tan Tock Seng Hospital, Singapore General Hospital, Changi General Hospital, Nihon University School of Medicine, Yonsei University Wonju College of Medicine and The Chinese University of Hong Kong.