MEDIA RELEASE
FOR IMMEDIATE RELEASE

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NEW STUDY LINKS GENETIC DIVERSITY OF TUMOURS WITH RESISTANCE TO TREATMENT IN ASIAN LUNG CANCER PATIENTS

The discovery can potentially lead to more precise treatments for Asian patients.

Singapore – Scientists from A*STAR's Genome Institute of Singapore (GIS) and medical oncologists from the National Cancer Centre Singapore (NCCS) have discovered that lung cancer tumours in Asian patients contain much higher genetic diversity than previously expected. Hence, this type of tumour tends to develop resistance despite initial tumour shrinkage. With this discovery, scientists and oncologists are better equipped to guide treatments and develop more refined and personalised approaches to common non-small-cell lung carcinoma (NSCLC). The study was published in the international journal *Nature Communications*.

Lung cancer is the most common cause of cancer mortality in the world. It accounts for approximately 19 percent of all cancer-related deaths worldwide and has a mortality rate more than twice that of any other cancer[1]. Lung cancer is also the most common type of cancer in Asia[2]. The number of incidences and deaths are expected to rise with increased pollution, particularly in large, densely populated Asian cities. Thus, newer and more effective individualised treatment strategies are crucial to tackle the growing threat and improve the quality of patients' lives.

Lung cancer in Asian patients is characterised by an important mutation in a gatekeeper gene known as the epidermal growth factor receptor, EGFR[3]. Gatekeeper genes, also known as the tumour suppressor genes, control and regulate cell cycles. It was discovered that mutations in this gene occur in more than 50 percent of the tumours in Singaporean lung cancer patients. While drugs targeting it are effective in controlling the disease, the response is short-lived. Most patients eventually succumb to cancer relapse in a matter of months or a few years. In some instances, patients do not even respond to these drugs at all. The variability in clinical outcomes, and the tumours' seemingly inevitable development of resistance to treatment, have intrigued doctors for years, and have remained major stumbling blocks in administering better patient care.

"This joint study is one of the first major efforts to characterise and identify lung tumours in Singaporean patients on a large scale. It has generated a treasure trove of new genetic information and enabled us to perform detailed analyses, leading us to conclude that lung

[1] http://www.who.int/mediacentre/factsheets/fs297/en/

[2] http://www.who.int/mediacentre/factsheets/fs297/en/

[3] The Epidermal Growth Factor Receptor (EGFR) is a gene that can result in cancer if it mutates. In a healthy cell, EGFR allows cells to grow and divide. When mutation occurs, as happens in cancer, the cancer cells continue to grow and divide uncontrollably, forming a mass of cells called a tumour. https://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/epidermal-growth-factor-receptor-egfr-testing-advanced-non-small-cell-lung-cancer

tumours in Asian patients are surprisingly more complex than previously appreciated," mentioned Dr Rahul Nahar, the first author of this study and a Research Associate at GIS.

"The study of the genetic complexity of tumours in Asian patients has provided us with new insights as to why they may quickly develop resistance after initial response to anti-EGFR drug inhibitors. We also found that tumours with a high number of drivers, mutations that cause cancer progression, tend to be associated with poor drug response," explained Dr Axel Hillmer, Principal Investigator at GIS and a co-corresponding author of this study.

"Understanding the comprehensive genetic landscape of these tumours allows us to go beyond single gene mutations (such as EGFR) to better understand the behaviour of individual tumours, and tailor treatments more effectively. Further work needs to be focused on identifying drug combinations or treatment strategies that take into account the tumours' ability to adapt to different treatments," said Dr Daniel Tan, Senior Consultant Medical Oncologist at NCCS and the corresponding author of this paper.

Professor Ng Huck Hui, Executive Director of GIS, said, "Timely and comprehensive research on disease states is critical, especially for diseases with a mortality rate as high as lung cancer. The study represents one of the first attempts at such an in-depth analysis of this unique subtype of NSCLC, and has yielded new insights and research directions. Discoveries like this will continue to pave the way for developing increasingly precise treatments."

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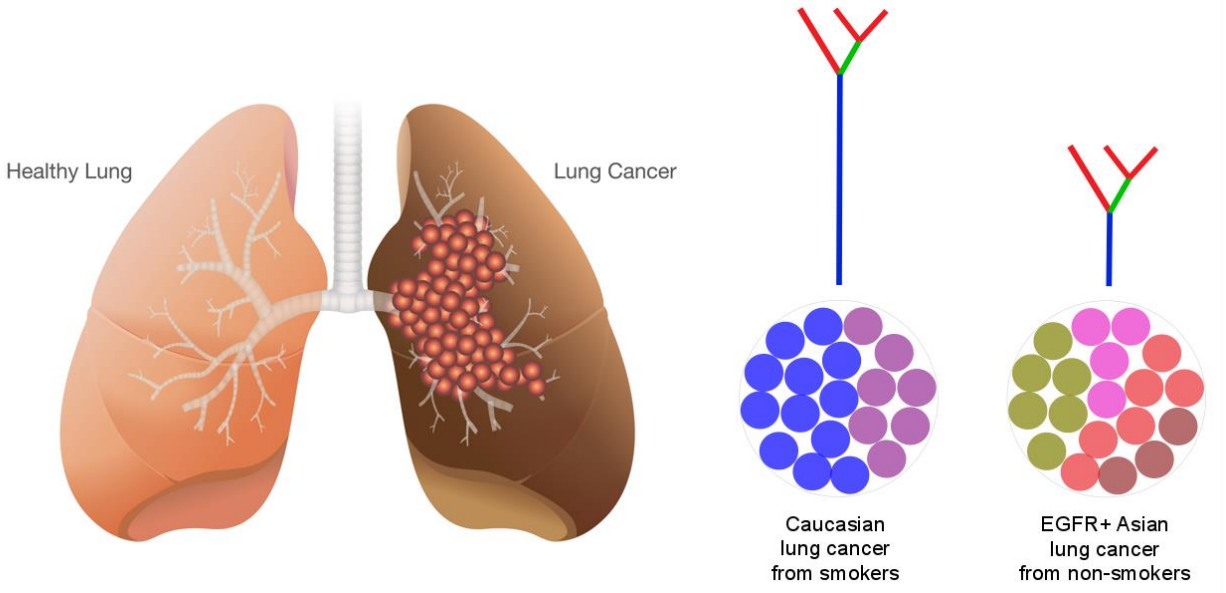
IMAGES



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Researchers from Singapore discovered that the EGFR mutant lung cancer in Asians is more varied than its counterpart observed in Caucasians. This suggests that genetic evolution is driving lung cancers into two groups differentiated by patients' ethnicities.

Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Nature Communications*, under the title, "Elucidating the genomic architecture of Asia EGFR-mutant lung adenocarcinoma through multi-region exome sequencing" by Rahul Nahar[1#], Weiwei Zhai[2#], Tong Zhang[2#], Angela Takano[3!], Alexis J. Khng[1!], Yin Yeng Lee[1!], Xingliang Liu[1], Chong Hee Lim[4], Tina P.T. Koh[4], Zaw Win Aung[5] ,Tony Kiat Hon Lim[3], Lavanya Veeravalli[6], Ju Yuan[9], Audrey S.M. Teo[1], Cheryl X. Chan[1], Huay Mei Poh[1], Ivan M.L. Chua[7], Audrey Ann Liew[8], Dawn Ping Xi Lau[8,11], Xue Lin Kwang[8,11], Chee Keong Toh[8], Wan-Teck Lim[8], Bing Lim[9], Wai Leong Tam[9], Eng-Huat Tan[8], Axel M. Hillmer[1,10*], Daniel S.W. Tan[8,9,11*].

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About A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.gis.a-star.edu.sg

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We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

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About National Cancer Centre Singapore (NCCS)
National Cancer Centre Singapore (NCCS) provides a holistic and multi-disciplinary approach to cancer treatment and patient care. We treat almost 70 per cent of the public sector oncology cases, and they are benefiting from the sub-specialisation of our clinical oncologists. NCCS is also accredited by the US-based Joint Commission International for its quality patient care and safety. To deliver among the best in cancer treatment and care, our clinicians work closely with our scientists who conduct robust cutting-edge clinical and translational research programmes which are internationally recognised. NCCS strives to be a global leading cancer centre, and shares its expertise and knowledge by offering training to local and overseas medical professionals. www.nccs.com.sg