JOINT NEWS RELEASE

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Study led by NTU Singapore and Chiba University finds that a common virus can trigger quicker growth of nasopharyngeal cancer

Scientists from **Nanyang Technological University, Singapore (NTU Singapore)** and **Chiba University** in Japan have shown how the Epstein-Barr virus (EBV) alters how specific genes are regulated, making nasopharyngeal cancer tumours (NPC) grow faster.

The Epstein-Barr virus, also known as human herpesvirus 4, is one of the most common human viruses[1], causing infectious mononucleosis, also known as mono or glandular fever, and other illnesses.

The researchers found that EBV tricks human cells into turning on specific genes that promote cancerous growth. Studying cells from patients with NPC, scientists observed how the virus acts as it infects nasopharynx cells[2] to 'switch on' genes that trigger the rapid multiplication of NPC cells.

This new study provides additional insight into the link between EBV and NPC. Although previous research has associated the two diseases, researchers have not convincingly demonstrated a definitive interaction between the virus and disease until now.

More than 130,000 new cases of NPC are diagnosed worldwide annually, with the majority of cases occurring in South-east Asia, China, and Northern Africa[3]. Men are three times more commonly affected than women.

In Singapore, the incidence of NPC is among the highest globally, with around 300 new cases diagnosed each year[4]. Detection typically occurs late due to mild or

[1] About Epstein-Barr Virus (EBV), The United States Centers for Disease Control and Prevention (2023).
[2] These cells found in the passageway located behind the nose, just above the throat, which connects the nose to the respiratory system.
[3] Nasopharyngeal Cancer Incidence and Mortality in 185 Countries in 2020 and the Projected Burden in 2040: Population-Based Global Epidemiological Profiling, JMIR Public Health and Surveillance (2023).
[4] Nasopharyngeal Cancer (Nose Cancer), HealthHub Singapore (2023).

nonspecific early symptoms, resulting in delayed diagnosis, poorer prognosis, and reduced treatment success rates.

The findings from the NTU-Chiba University team could lead to new treatments for NPC by targeting the genes affected by EBV. This would involve developing treatments that specifically interfere with the activity of these genes, such as drugs or therapies that block the function of the genes that EBV activates, thereby preventing tumour growth or even killing cancer cells.

The samples of NPC and normal nasopharyngeal cells were obtained from 25 patients at the Division of Otolaryngology and Head and Neck Surgery, Kanazawa University Hospital.

Co-lead author Associate Professor Melissa Jane Fullwood, from NTU's School of Biological Sciences, who led the study, said: "Our study delves into the nuanced relationship between EBV and NPC. Through analysis of EBV-infected NPC cells and comparison with healthy nasopharyngeal cells, we identified crucial mechanisms underlying the disease progression. By shedding light on these intricate processes, our findings not only expand scientific knowledge but also offer practical implications for future therapeutic strategies, contributing to advancements in clinical care and improved outcomes for patients that suffer from this deadly form of cancer."

Lead author of the study, Professor Atsushi Kaneda from the Graduate School of Medicine, Chiba University, Japan, said: "In cells, certain sections of the genetic material are actively involved in cell functions, while others remain dormant. Our research revealed that the Epstein-Barr virus (EBV) attaches itself to these dormant sections within NPC cells. This abnormal attachment triggers the activation of these dormant sections, ultimately contributing to the development of NPC."

Providing an independent comment on the study, **Associate Professor Joanne Ngeow**, **who is Associate Professor in Genomic Medicine at NTU's LKCMedicine,** said: "Clinicians need to better understand why cancers arise so that we can better treat and advocate for prevention. This study is a landmark study not only because it helps us understand how EBV virus interacts with host genetics for NPC development but also paves the way for future understanding of other virus-induced cancers" Assoc Prof Ngeow is also **Senior Consultant at the Division of Medical Oncology from the National Cancer Centre Singapore.**

The study, which represents an advance in understanding how our bodies respond to infections, reflects NTU's commitment to responding to the needs and challenges of healthy living and ageing, one of humanity's grand challenges that the University seeks to address through its **NTU 2025 strategic plan**.

The study also saw participation from researchers from Kanazawa University and Hamamatsu University, Japan and the Duke-NUS Medical School, Singapore. The findings were published recently in the peer-reviewed journal *eBioMedicine*.

A trojan horse that changes cells from within

Although the Epstein-Barr virus does not always cause illness in humans, as our immune systems can quickly detect when the virus affects cells, it lays dormant in our bodies. It primarily spreads between people through bodily fluids, particularly saliva.

The virus's genetic material typically remains inactive because it is not actively engaged in processes within its external environment. However, upon infecting a host cell, the virus enters a new environment that triggers changes in its behaviour. The host cell provides the necessary factors and conditions for the virus's genetic material to become active.

The virus activates human genes that were previously switched off, causing cells to grow uncontrollably and form tumours. Additionally, EBV can activate cellular DNA switches called 'enhancers,' which regulate how genes are expressed.

This abnormal activation of enhancers leads to further abnormal gene activity, promoting the growth and development of NPC tumours. Furthermore, EBV's interaction with the host's genetic material promotes changes in the host's DNA structure, activating both viral and host genes that contribute to tumour growth.

Assoc Prof Fullwood added: "EBV is surprisingly common in humans, affecting a significant portion of the population. Its ability to interact with our cells and interfere with various diseases underscores the intricate relationship between viruses and human health. Understanding how these microscopic viruses influence our biology opens pathways to comprehend the broader impact of viral infections on our well-being, paving the way for new insights into disease prevention and treatment."

Prof Kaneda added: "We hypothesise that the idea of enhancer infestation, which rewires DNA structure and activates nearby genes, could offer new insight into how cancer forms. This involves the interaction of viral DNA with changes in how DNA is arranged in cells, which might be important for many types of cancer, not just those linked to EBV."

The NTU-Chiba University team is in discussion with pharmaceutical companies and hopes to develop therapies focussing on the genes that EBV targets in nasopharyngeal cells.

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Notes to Editor:

The research paper titled: "*Enhancer infestation drives tumorigenic activation of inactive B compartment in Epstein-Barr virus-positive nasopharyngeal carcinoma*" *was* published in *eBioMedicine* in Mar 2024. DOI 10.1016/j.ifset.2023.103551

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Media contact:

Mr Joseph Gan
Manager, Media Relations
Corporate Communications Office
Nanyang Technological University, Singapore
Email: joseph.gan@ntu.edu.sg

Ms Momoko Watanabe
Public Relations Division
Chiba University
Tel: +81-43-290-2018
Email: koho-press@chiba-u.jp

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 and Singapore Centre for Environmental Life Sciences Engineering – and various leading research centres such as the Earth Observatory of Singapore, Nanyang Environment & Water Research Institute 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, NTU

has achieved 100% Green Mark Platinum certification for all its eligible building projects. 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 Chiba University

Chiba University boasts 11 faculties and 19 graduate schools on 5 campuses and a rich academic environment where students can acquire a broad-based interdisciplinary education as well as an advanced level of expertise. While respecting diversity in learning, Chiba University promotes innovative research through collaboration and researcher support programs, leading to the development of new fields of research, which will continue to make a wide range of social contributions both locally and internationally.

https://www.chiba-u.ac.jp/e/index.html