



## **JOINT NEWS RELEASE**

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### **NTU Singapore and Oxford study discover new process for cells to repair DNA damage**

A team of international researchers at the **University of Oxford (Oxford)** and **Nanyang Technological University, Singapore (NTU Singapore)**, has discovered a new process for repairing damaged DNA that is particularly relevant for patients undergoing colorectal cancer treatments.

Reporting their finding in *Cell*, the researchers describe a new process in DNA repair in which cells remove harmful DNA-protein lesions from a cell's nucleus, ensuring the stability of their genetic material and promoting cell survival. The team calls this new process **nucleophagy**.

Nucleophagy is a natural cellular cleaning mechanism known as autophagy that is essential for repairing DNA and ensuring cell survival. It involves a commonly expressed protein called **TEX264**.

In a patient receiving chemotherapy for colorectal cancer, the drugs cause DNA lesions to form. In response, the body expresses TEX264, which activates the nucleophagy process, guiding the lesions to the cell's waste disposal system, where they are broken down and destroyed.

The research team used advanced techniques, including biochemical, cell biological and bioinformatics tools, zebrafish animal model and colorectal cancer patient materials, to confirm that nucleophagy is crucial for repairing damaged DNA.

This study provides insights into a new pathway for cells to repair DNA damage, which could improve cancer treatments and lead to better outcomes for patients in future, says the research team, which comprises scientists and clinicians.

Lead investigator **Kristijan Ramadan, the Toh Kian Chui Distinguished Professor in Cancer and Stem Cell Biology, and Director of Cancer Discovery and Regenerative Medicine Programme at Lee Kong Chian School of Medicine**

**(LKCMedicine), NTU Singapore**, said, “While autophagy is known to be associated with DNA repair, there has been no evidence of its direct role in the repair of DNA lesions until now.”

“Our discovery that nucleophagy plays a direct role in DNA repair of chemotherapy-induced lesions is the result of a five-year joint effort among several laboratories in the UK, Singapore, USA, Portugal and Croatia,” added Prof Ramadan, who is also **Medical Research Council Investigator at the Department of Oncology, Oxford**.

### **Patients with high levels of TEX264 have better responses to cancer treatment**

In particular, the research team says the findings are significant for patients with colorectal cancer – the second leading cause of cancer-related deaths worldwide, according to the World Health Organisation.

An analysis of colorectal cancer patients treated with Topoisomerase 1 inhibitors, such as FOLFIRI therapy (a common chemotherapy used to treat colorectal cancer), showed that patients with high levels of TEX264 in their tumours have a 50 per cent better response to treatment compared to those with low levels of TEX264.

**First author of the study, Oxford’s Oncology DPhil student Pauline Lascaux**, said, “This novel mechanism of DNA damage repair helps us comprehend how our cells maintain genetic integrity and respond to cancer treatments. This breakthrough opens avenues for a better understanding of how our body protects genetic material and how we can enhance the efficacy of cancer therapies for patients. I believe that modulating autophagy activity is the key to overcoming resistance to therapy in colorectal cancer.”

Commenting as an independent expert, **Dr Jens Samol, Senior Consultant in Medical Oncology, Department of Medical Oncology, Tan Tock Seng Hospital, Singapore**, said, “Prof Ramadan and his international research team made a fascinating breakthrough discovery called nucleophagy, which could be a game-changer for more than just colorectal cancer patients. Some cancer treatments, like camptothecin and its variations, are already used to treat cancers like bowel, pancreas, ovarian, breast, and certain types of lung cancers. This new finding could help doctors better understand why some cancers resist treatment and pave the way for more effective therapies in the future.”

In future studies, the research team will explore the role of nucleophagy in the body’s response to chemotherapeutic drugs for other cancers, to see if their discovery is further validated. The team’s ultimate goal is to use this discovery to improve current chemotherapy responses for cancer patients.

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## Notes to Editor:

Paper titled "[TEX264 drives selective autophagy of DNA lesions to promote DNA repair and cell survival](https://doi.org/10.1016/j.cell.2024.08.020)" published in *Cell*, 11 September 2024  
<https://doi.org/10.1016/j.cell.2024.08.020>



Image: DNA (in blue) and the nuclear envelope (in green) found in the nuclei of cancer cells are attacked by the lysosomes (in red) after exposure to chemotherapy drugs as part of the nucleophagy-orchestrated DNA repair process.

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### ***About Nanyang Technological University, Singapore***

A research-intensive public university, Nanyang Technological University, Singapore (NTU Singapore) has 35,000 undergraduate and postgraduate students in the Business, Computing & Data Science, Engineering, Humanities, Arts, & Social Sciences, Medicine, Science, 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](http://www.ntu.edu.sg)

### ***About the University of Oxford***

Oxford University has been ranked number 1 in the Times Higher Education World University Rankings for the eighth year running and number 3 in the QS World Rankings 2025. At the heart of this success are the twin pillars of our ground-breaking research and innovation and our distinctive educational offer.

Oxford is world-famous for research and teaching excellence and is home to some of the most talented people from across the globe. Our work helps the lives of millions, solving real-world problems through a vast network of partnerships and collaborations. The breadth and interdisciplinary nature of our research, alongside our personalised approach to teaching, spark imaginative and inventive insights and solutions.