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Study identifies mechanism that helps prevent cancer, neurodegeneration, and premature aging

News Medical

Researchers at the University of Oxford and Nanyang Technological University, Singapore (NTU Singapore) have uncovered the mechanism by which cells identify and repair a highly toxic form of DNA damage that causes cancer, neurodegeneration, and premature aging.

The findings, published in Nucleic Acids Research, reveal how DNA-protein crosslinks (DPCs) - harmful DNA lesions induced by chemotherapy, formaldehyde, and UV exposure - are recognised and broken down by SPRTN, a key repair enzyme.

The research team discovered a new region within SPRTN that enables it to selectively target DPC lesions, increasing its repair activity 67-fold while leaving surrounding structures unharmed.

Led by Kristijan Ramadan, Toh Kian Chui Distinguished Professor in Cancer and Stem Cell Biology at the Lee Kong Chian School of Medicine, NTU Singapore and Honorary Senior Researcher at the Department of Oncology, University of Oxford, the work has important implications for improving cancer therapy and healthy aging.

The threat of DPC lesions

Every time a cell divides into two, it must accurately create a copy of all its DNA, a process that involves the tight coordination of sophisticated molecular machinery. DNA-protein crosslinks (DPCs) are bulky lesions in which unwanted proteins attach to DNA, blocking the process of copying the cell's DNA.

If left unrepaired, DPCs can cause neurodegeneration, premature aging, and cancer. Therefore, understanding how these lesions are repaired is crucial for protecting genome integrity and preventing these conditions.

DPCs can occur through normal cellular metabolism, as well as exposure to chemotherapeutic drugs, UV radiation, and environmental agents like formaldehyde. Formaldehyde is a Group 1 carcinogen commonly found in household furniture, paint, and air pollution, including haze.

SPRTN is a critical enzyme that protects cells against DPC lesions. It travels along the DNA and degrades the proteins in the lesions, which clears the blockage and enables the DNA copying process to proceed.

Until now, it was unknown how SPRTN specifically breaks down DPC lesions without damaging functional proteins in the cell.

Read the full story here.

https://www.msn.com/en-gb/health/other/study-identifies-mechanism-that-helps-prevent-cancer-neurodegeneration-and-premature-aging/ar-AA1J0Pl2