

Recipe for perfect balance of breaks and repairs in our genome could help fight cancer

June 12 2018



Credit: CC0 Public Domain

Scientists at the University of Sheffield have discovered what keeps the perfect balance of breaks and repairs in our DNA—something which could help improve the success of chemotherapy and combat neurodegeneration associated with ageing.

Our genome, where precious genetic information is stored, is challenged

with thousands of breaks every day.

Cells possess an army of proteins that search for, detect and fix these breaks to maintain genome integrity, but little is known about how the cell fine-tunes the level of response in these [repair](#) factories to suit each and every repair event.

The level of proteins in our [cells](#) is controlled by synthesis and degradation. Cells get rid of proteins when not needed by attaching a small peptide called ubiquitin.

The new study, led by Dr. Sherif El-Khamisy at the University of Sheffield's Department of Molecular Biology and Biotechnology, has revealed an enzyme called UCHL3, which controls DNA repair by removing ubiquitin marks from TDP1—a DNA repair protein. The findings also have implications in brain ageing which has an affect on memory, cognitive function and learning.

An overexpression of UCHL3 causes less ubiquitination of TDP1 and increases its [protein](#) level, which is found in chemotherapy resistant cancers such as rhabdosarcoma—the most common [soft tissue sarcoma](#) in children, which has a debilitating effect on the muscles, tendons and cartilage.

Too little UCHL3, however, was found to cause more ubiquitination of TDP1 reducing its level in [neurological diseases](#) such as ataxias—a group of disorders that affect co-ordination, balance and speech.

Dr. El-Khamisy said: "This study identifies UCHL3 as a novel therapeutically druggable target where suppression of its activity can improve cancer treatment, whereas encouraging and fuelling its activity can combat neurodegeneration.

"Defective DNA repair is a common theme in a number of neurological disorders including [motor neuron disease](#) and dementia. Finding novel approaches to fuel the cell's ability to repair genomic breaks may hold promise in improving treatment of a broad range of neurological diseases."

The five-year study is funded by a Wellcome Trust Investigator Award to Dr. El-Khamisy and involved collaborations across departments at The University of Sheffield and internationally.

The full study is published today (12 June 2018) in the journal *Cell Reports*.

Provided by University of Sheffield

Citation: Recipe for perfect balance of breaks and repairs in our genome could help fight cancer (2018, June 12) retrieved 19 April 2024 from <https://medicalxpress.com/news/2018-06-recipe-genome-cancer.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.