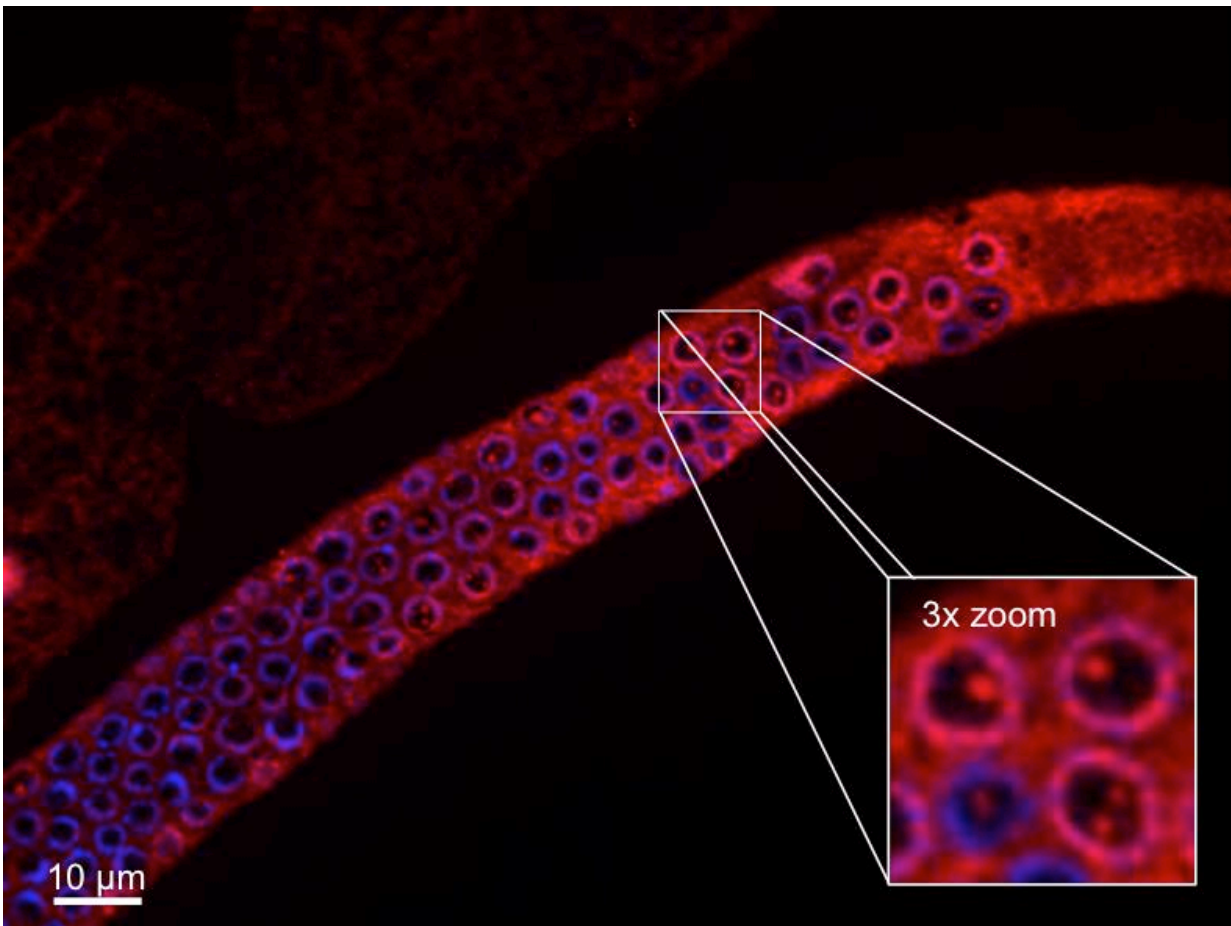


New switch decides between genome repair and death of cells

September 27 2016



Isolated germ line of *C. elegans*. Credit: University of Cologne

The genetic information of every cell is encoded in the sequence of the

DNA double helix. Double strand breaks in the DNA, which can be induced by radiation, are a dangerous threat to the cells, and if not properly repaired can lead to cancer. Damaged cells need to decide whether the breaks can be fixed or whether they should be removed by a cellular suicide program called "apoptosis" before initiating cancer.

Björn Schumacher, one of the senior authors, explains: "Within seconds after an harmful incident, different mechanisms start. In a schizophrenic way, the cell starts repairing as well as preparing for apoptosis. We identified an uncharacterized mechanism that integrates signals from the ongoing repair process and the cell death machinery. A protein called UFD-2 forms large complexes at the breaks and verifies whether to proceed with the repair or whether it's time to die." In the process, UFD-2 is a point of intersection that both receives and gives signals.

The experiments were performed with the nematode *Caenorhabditis elegans*. "For our research we used different strains of *C. elegans*, including wild type and genetically modified ones. They were exposed to ionizing radiation to induce double strand breaks and then examined," says Leena Ackermann, lead author of the study. Schumacher adds: "The results are important to further understand how and why a cell decides to repair or to die. Is the repair still ongoing and successful or is apoptosis necessary? Cells lacking UFD-2 fail to undergo apoptosis. In humans such a situation could lead to a higher risk of a damaged cell becoming a cancer cell."

All the proteins that play a part in this mechanism can be found in humans as well, and the findings could be highly relevant to better understanding how DNA damage leads to cancer. DNA damage is also an important driver of the aging process. Although apoptosis protects from cancer, excessive cell death can lead to tissue degeneration and aging. The senior author Thorsten Hoppe originally identified UFD-2 as a key regulator of protein degradation. Here, UFD-2 forms

regulatory centers that coordinate DNA repair and cell death.

Hoppe hopes for resulting advances in tumor therapy: "The knowledge we gained from this study provides new perspectives for fighting cancer pharmaceutically. It might be possible to manipulate the well-balanced process of apoptosis and protein degradation to make clearance of tumor cells more efficient."

More information: Leena Ackermann et al. E4 ligase–specific ubiquitination hubs coordinate DNA double-strand-break repair and apoptosis, *Nature Structural & Molecular Biology* (2016). [DOI: 10.1038/nsmb.3296](https://doi.org/10.1038/nsmb.3296)

Provided by University of Cologne

Citation: New switch decides between genome repair and death of cells (2016, September 27) retrieved 18 April 2024 from <https://phys.org/news/2016-09-genome-death-cells.html>

<p>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.</p>
--