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Toward a better understanding of the mechanisms blocking cancer cell growth

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DNA damage can lead to gene inactivation or deregulation and cause various diseases such as cancer; however, many DNA repair mechanisms allow cells to survive against such damage. A study lead by Antoine Simoneau of the laboratory of Dr. Hugo Wurtele, a researcher in immunology-oncology at the Maisonneuve-Rosemont Hospital (CIUSS de l'Est-de-l'Île-de-Montréal) and professor at the Faculty of Medicine, University of Montreal, and recently published in the prestigious journal *Nucleic Acids Research*, provides valuable information about certain mechanisms governing DNA repair. The study is a collaboration between several institutions and opens the way to better understand the mechanisms of action of drugs that prevent cancer cell growth.

To adapt to the small size of cell nuclei, DNA wraps around proteins called histones to form chromatin. Cells can chemically modify histones so as to change chromatin structure and thereby control the various functions of DNA. Recent research has shown that new drugs that inhibit histone deacetylases (HDACs), which affect chromatin, are promising for cancer treatment.

The study by Dr. Wurtele's research team and collaborators used yeast as a model system to understand, at a molecular level, the mechanisms that influence cell growth in the presence of a particular class of HDACs.

The experiments demonstrate that Class III HDACs, which influence various cellular processes involved in carcinogenesis and response to chemotherapy agents, strongly block cell proliferation by preventing the

normal functioning of various factors involved in the response to DNA damage spontaneously generated by cellular metabolism.

"This basic research allows for a better understanding of the overall effects of HDAC inhibitors on cells and can eventually lead to an optimization of their clinical use," said Dr. Wurtele.

These findings will guide future research at Dr. Wurtele's laboratory to determine how this new class of drugs inhibits the growth of cancer cells.

More information: Antoine Simoneau et al. Chromosome-wide histone deacetylation by sirtuins prevents hyperactivation of DNA damage-induced signaling upon replicative stress, *Nucleic Acids Research* (2016). DOI: 10.1093/nar/gkv1537

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