New DNA research reveals undiscovered white dots on the map

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Researchers at the University of Copenhagen have located a previously unknown function in the so-called histones, which allows for an improved understanding of how cells protect and repair DNA damages. This knowledge may eventually result in better treatments for diseases such as cancer.

The researchers have discovered a hitherto unknown function in the so-called histones, which can contribute to better treatments for diseases caused by cellular changes.

"I believe that there's a lot of work ahead. It's like opening a door onto a previously undiscovered territory filled with lots of exciting knowledge.

The histones are incredibly important to many of the cells' processes as well as their overall wellbeing," says Niels Mailand from the Novo Nordisk Foundation Centre for Protein Research at the Faculty of Health and Medical Science.

This new discovery may be of great importance to the treatment of diseases caused by cellular changes such as cancer and immune deficiency syndrome. The findings have just been published in the scientific journal, *Nature*.

Histones enable the tight packaging of DNA strands within cells. The strands are two metres in length and the cells usually approx. 100,000 times smaller. Generally speaking, there are five types of histones. Four of them are so-called core histones, and they are placed like beads on the DNA strands, which are curled up like a ball of wool within the cells. The role of the histones is already well described in research, and in addition to enabling the packaging of the DNA strands they also play a central part in practically every process related to the DNA-code, including repairing possibly damaged DNA.

Effective treatment

The four core histones have so-called tails, and among other things they signal damage to the DNA and thus attract the proteins that help repair the damage. Between the histone "yarn balls" we find the fifth histone, Histone H1, but up until now its function has not been thoroughly examined.

Using a so-called mass spectrometer, a technique developed in collaboration with fellow researchers at the Novo Nordisk Foundation Centre for Protein Research, Niels Mailand and his team have discovered that, surprisingly, the H1 histone also helps summon repair proteins.

"In international research, the primary focus has been on the core histones and their functionality, whereas little attention has been paid to the H1 histone, simply because we weren't aware that it too influenced the repair process. Having discovered this function in the H1 constitutes an important piece of the puzzle of how cells protect their DNA, and it opens a door onto hitherto unknown and highly interesting territory," Niels Mailand elaborates.

He expects the discovery to lead to increased research into Histone H1 worldwide, which will lead to increased knowledge of cells' abilities to repair possible damage to their DNA and thus increase our knowledge of the basis for diseases caused by cellular changes. It will also generate more knowledge about the treatment of these diseases.

"The knowledge we generate can prove important to the development of more targeted treatments for diseases caused by cellular changes, including cancer. By mapping the function of the H1 histone, we will also learn more about the repair of DNA damages on a molecular level. In order to provide the most efficient treatment, we need to know how the cells prevent and repair these damages," Niels Mailand concludes.

More information: Tina Thorslund et al. Histone H1 couples initiation and amplification of ubiquitin signalling after DNA damage, *Nature* (2015). DOI: 10.1038/nature15401

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