Oxidative DNA damage repair

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Oxidative stress damages DNA. Researchers in the Vetsuisse Faculty have now decoded the mechanism that repairs DNA damaged in this way. This repair mechanism could lead to less invasive approaches in cancer therapy and contribute to the development of new tests for the early diagnosis of cancer.

Oxidative stress is the cause of many serious diseases such as cancer, Alzheimer's, arteriosclerosis and diabetes. It occurs when the body is exposed to excessive amounts of electrically charged, aggressive oxygen compounds. These are normally produced during breathing and other metabolic processes, but also in the case of ongoing stress, exposure to UV light or X-rays. If the oxidative stress is too high, it overwhelms the body's natural defences. The aggressive oxygen compounds destroy genetic material, resulting in what are referred to as harmful 8-oxo-guanine base mutations in the DNA.

Together with the University of Oxford, Enni Markkanen, a veterinarian in the working group of Prof. Ulrich Hübscher from the Institute of Veterinary Biochemistry and Molecular Biology at the University of Zurich has decoded and characterized the repair mechanism for the mutated DNA bases. This mechanism efficiently copies thousands of 8-oxo-guanines without their harmful mutations, thus normally preventing the negative consequences of 8-oxo-guanine damage. In their study, published in *PNAS*, the researchers outline the detailed processes involved in the local and temporal coordination of this repair mechanism.

Prof. Ulrich Hübscher hopes that this basic research can be used therapeutically. "We expect that the DNA repair mechanism discovered here will lead to less invasive approaches in cancer therapy and that it will be possible to develop new clinical tests for the early detection of certain types of cancer." In cooperation with University Hospital Zurich, a study is already underway that involves examining samples of different types of cancer for the repair gene and its regulation.

More information: Enni Markkanen, Barbara van Loon, Elena Ferrari, Jason L. Parsons, Grigory L. Dianov, and Ulrich Hübscher. Regulation of oxidative DNA damage repair by DNA polymerase λ and MutYH by crosstalk of phosphorylation and ubiquitination. *Proceedings of the American Academy of Sciences. PNAS.* December 26, 2011. www.pnas.org/cgi/doi/10.1073/pnas.1110449109

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