

Molecular corkscrew

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Scientists from the universities of Zurich and Duisburg-Essen have discovered a specific function of the protein p97/VCP. They demonstrate that the protein repairs DNA breaks like a corkscrew, a repair mechanism that could also prove significant for cancer therapy.

Human genetic material is constantly at risk of injury from the environment. Possible causes of damage include metabolic processes, chemical substances or ionizing radiation, such as X-radiation. Even a low dose of radiation can cause breaks in the [DNA double helix](#). Normally, these DNA breaks are repaired by the body's own proteins, but they can also cause cancer if the repair is unsuccessful.

The protein p97/VCP plays a key role in repairing DNA breaks. The research groups headed by Kristijan Ramadan from the University of Zurich's Institute of Veterinary Pharmacology and Hemmo Meyer from the University of Duisburg-Essen have discovered that p97/VCP aids DNA repair like a corkscrew. Proteins that accumulate at the break site are initially marked with remnants of the protein ubiquitin. These remnants bind to the p97/VCP protein and are removed like a cork. For the [DNA repair](#) to be completed successfully, the precise spatial and temporal removal of the [repair proteins](#) from the damage site is crucial.

The repair mechanism with p97/VCP and its inhibition could be important for cancer therapy. "By blocking p97/VCP's corkscrew activities, it should be possible to increase the impact of radio- or chemotherapy," says veterinary pharmacologist Kristijan Ramadan. Radiation causes extensive, often fatal damage to cancer cell DNA. The

therapeutic effect could be improved further if, at the same time, the repair mechanism usually deployed in [cancer cells](#) were to be inhibited with p97/VCP. "Maybe the [radiation dosage](#) with all its unpleasant side effects could even be reduced," concludes Ramadan.

More information: Mayura Meerang, Danilo Ritz, Shreya Paliwal, Zuzana Garajova, Matthias Bosshard, Pavel Janscak, Ulrich Hübscher, Hemmo Meyer, and Kristijan Ramadan. The ubiquitin selective remodeling factor p97/VCP orchestrates the DNA damage response. *Nat Cell Biol.* October 23, 2011. [doi: 10.1038/ncb2367](https://doi.org/10.1038/ncb2367)

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