New insight into cancer drug resistance mechanism

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Research from the laboratory of Dr. Edgar Hartsuiker at the Bangor North West Cancer Research Institute, School of Medical Sciences, has been published in the latest issue (29 May) of the high-ranking journal *Science Advances*.

Many cancer drugs kill cancer cells by inhibiting the replication of their genetic material, the DNA. One of these drugs is Gemcitabine, used to treat, among others, pancreatic, bladder and lung cancer. Gemcitabine mimics one of the building blocks of DNA, the nucleoside deoxycytidine, and competes with it for integration into cancer cell DNA. Once integrated, it inhibits DNA replication and thus division of the cancer cell.

The Hartsuiker lab has discovered that a protein called Mre11 is able to remove Gemcitabine from the DNA, allowing replication to continue, thus uncovering a novel Gemcitabine resistance mechanism.

Dr. Edgar Hartsuiker explains: "As Mre11 is frequently mutated in cancer cells, this knowledge might be exploited in the future for cancer therapy by guiding new treatment regimens and/or the development of novel cancer drugs. We have already initiated the drug discovery process, and have identified several compounds that inhibit the activity of Mre11."

More information: L. Boeckemeier et al. Mre11 exonuclease activity removes the chain-terminating nucleoside analog gemcitabine from the nascent strand during DNA replication, *Science Advances* (2020). DOI: 10.1126/sciadv.aaz4126

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