Substance interfering with the cells handling of protein waste could become new cancer drug

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(Medical Xpress) -- Researchers at Karolinska Institutet have identified a new kind of cancer drug that has been shown to be effective against tumours in different experimental systems. An article published in *Nature Medicine* shows that the new type of drug blocks the machinery that the cell uses to break down defective proteins.

Tumor cells have several genetic mutations, one of the effects of which is unbridled cell growth. One of the tumor cell's "weak spots" is that large amounts of defective proteins are produced. These proteins are broken down by proteasomes, the cell's "waste disposal units" for proteins. The researchers have identified a molecule called b-AP15 which inhibits the cell's ability to feed the protein waste into the proteasomes. The waste then accumulates, which leads to the death of the tumour cells via apoptosis. More precisely, b-AP15 inhibits the deubiquitinating enzymes USP14 and UCHL5 of the proteasomes. The study demonstrates that b-AP15-inhibited tumour growth in four separate animal models, which suggests that the substance could be used for treating cancer.

The substance was also shown able to kill off tumor cells that are resistant to a currently used cancer drug that inhibits the proteasome by another mechanism.

"This newly discovered mechanism of action is very promising," says

Stig Linder, professor of experimental oncology at the Department of Oncology and Pathology at Karolinska Institutet. "However, I should like to stress that we're unable to treat patients with our substances at present. But we hope that our continuing work will eventually lead to the development of new drugs."

Provided by Karolinska Institutet