

New method promises fewer side effects from cancer drugs

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His-tag acylation can accurately target complex yarn-like protein structures and also makes it possible to produce drugs with entirely new characteristics. Credit: Pexels

Protein research is one of the hottest areas in medical research because proteins make it possible to develop far more effective pharmaceuticals for the treatment of diabetes, cancer and other illnesses.

However, while proteins have great potential, they also present great challenges for scientists. Proteins have incredibly complex chemical

structures that make them difficult to modify. As a result, researchers have been looking for a tool to modify them more precisely without increasing a potential drug's side-effects.

"We often run the risk of not being approved by health authorities because [protein](#)-based drugs lack precision and may have side-effects. Among other things, this is because of the serious limitations with the tools that have been used up until now," says Professor Knud J. Jensen of the University of Copenhagen's Department of Chemistry.

Together with his research colleague, Sanne Schoffelen, he has developed a new protein-modifying method that promises fewer side-effects and could be pivotal in furthering the development of protein-based pharmaceuticals. Their work has been published in the distinguished journal, *Nature Communications*.

Protein structure is like an intricate ball of yarn

Researchers call the method His-tag acylation. Among other things, it makes it possible the addition of a toxic molecule to proteins that can attack sick cells in a cancer-stricken body without attacking healthy ones.

"Proteins are like a ball of yarn, a long thread of amino acids, which are turned up. This method allows us to precisely target these intricate structures, as opposed to making uncertain modifications when we don't know what is being hit within the ball of yarn. In short, it will help produce drugs with far more confidence about where modifications are being made, so that side effects can be minimized in the future," says Knud J. Jensen.

Modified proteins must target precisely

The fact that His-tag acylation can accurately target these complex yarn-like protein structures also makes it possible to produce drugs with entirely new characteristics.

For example, researchers can now attach a fluorescent molecule to proteins in such a way that a microscope can be used to track a protein's path through cells. The primary function of these proteins is to transport cancer fighting molecules around to sick cells, so it is important to carefully follow their path throughout the body in order to safely produce medications that don't have unintended side-effects.

More information: Manuel C. Martos-Maldonado et al, Selective N-terminal acylation of peptides and proteins with a Gly-His tag sequence, *Nature Communications* (2018). [DOI: 10.1038/s41467-018-05695-3](https://doi.org/10.1038/s41467-018-05695-3)

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