Enzymes from dangerous bacteria turn into important tools for protein chemistry

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Philipp Ochtrop from Umeå University has worked on a project to turn the two enzymes AnkX and Lem3 from the disease causing bacteria Legionella pneumophila into a valuable tool for the chemical modification of proteins. This new approach for protein functionalization can enable scientists to investigate protein function and develop new drugs against life threatening diseases.

The new technique, which is described in the doctoral thesis of Philipp Ochtrop, is based on an enzymatic reaction called phosphocholination. The phosphocholination is catalyzed by the protein AnkX, which uses a small organic molecule called CDP-choline to transfers a phosphocholine group to host cell proteins and thereby manipulate its function. The phosphocholination is part of several specific chemical reactions that are used by Legionella pneumophila to overtake a host cell after infection and turn it into a suitable environment for its multiplication. These events consequently lead to the outbreak of severe pneumonia.

"The interesting thing about the chemistry of intracellular bacteria is that it is so different in comparison to human cell's chemistry. This is a unique chance to use enzymes from bacteria in biochemistry, cell biology and biotechnology without having overlapping reactivity with human cells' enzymes," says supervisor Christian Hedberg.

The idea to use AnkX for labeling proteins arose by coincidence during studies on how AnkX modifies certain proteins with phosphocholine.

The experiments revealed that AnkX did not care particularly about the three-dimensional structure of its target proteins, but only recognized a short amino acid sequence in the protein. This discovery lead to the conclusion that any protein could be modified by AnkX, as long as the correct amino acid recognition sequence is added genetically.

"In combination with CDP-choline analogues that we prepared synthetically, the developed strategy can be exploited to reversibly functionalize proteins of interest with an array of useful chemical and biophysical handles", says Philipp Ochtrop.

"A future potential medical use for our results can be the selective labeling of antibodies with specific drugs that are consequently directed to cancer cells and kill them. This approach would be highly beneficial and reduce common side effects that are displayed by conventional cancer therapy."

Philipp Ochtrop has performed his studies in a close and highly interdisciplinary collaboration with a team of researchers led by Professor Aymelt Itzen from the Technical University in Munich.

More information: Selective protein functionalisation via enzymatic phosphocholination. umu.diva-portal.org/smash/get/ … 47446/FULLTEXT01.pdf

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