New light-tuned chemical tools control processes in living cells

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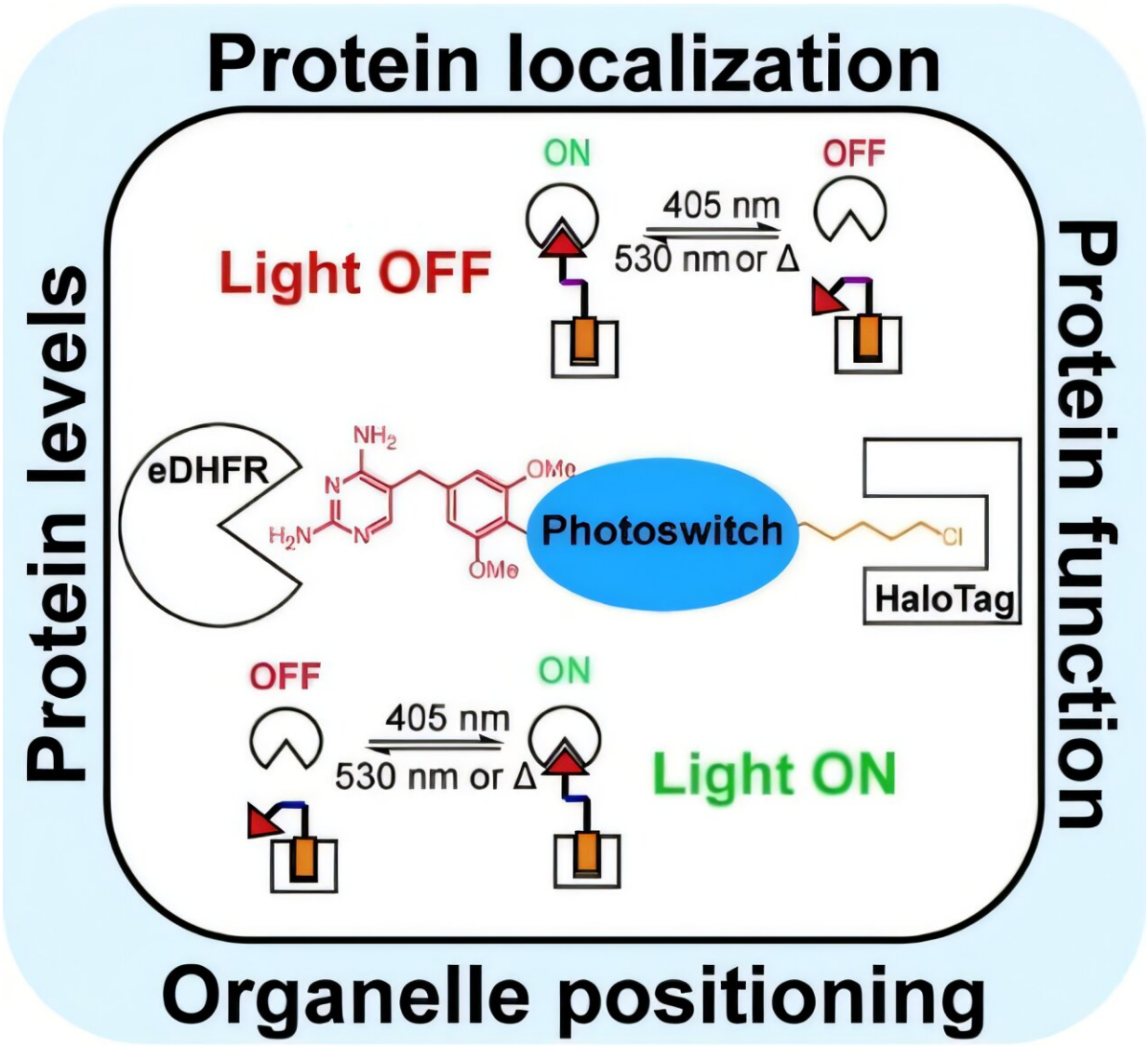


Credit: *Angewandte Chemie International Edition* (2025). DOI: 10.1002/anie.202416456

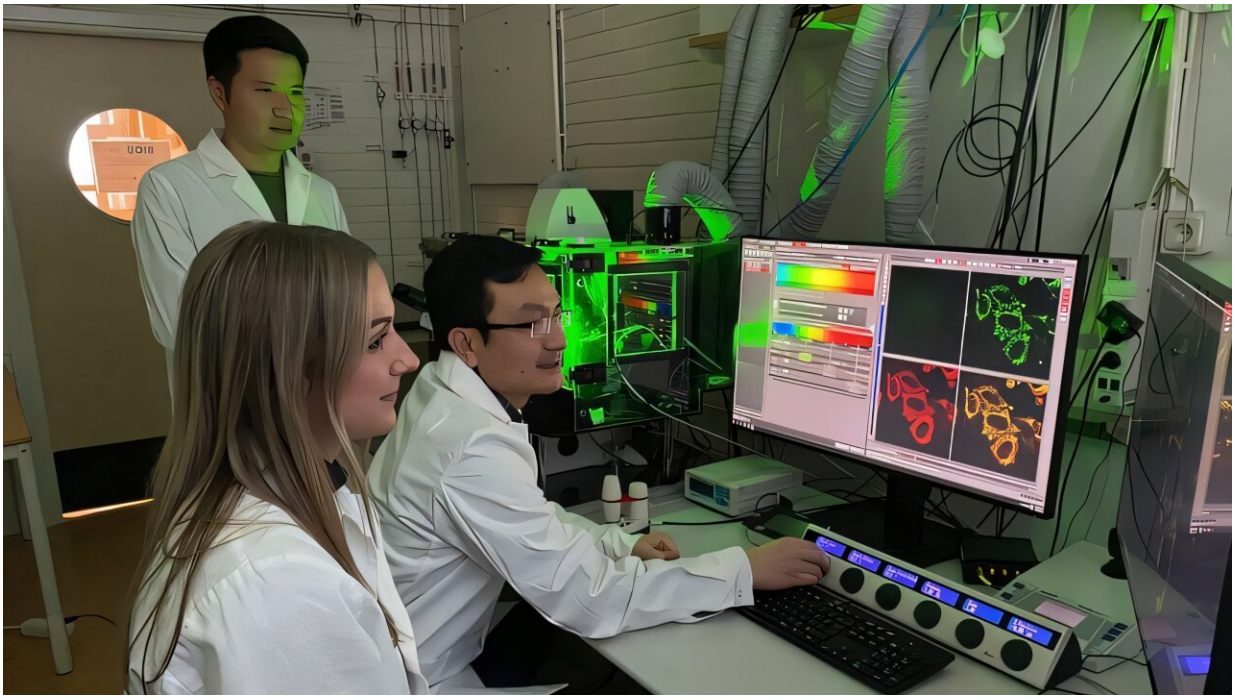
A research group at Umeå University has developed new advanced light-controlled tools that enable precise control of proteins in real time in living cells. This research opens doors to new methods for studying complex processes in cells and could pave the way for significant advances in medicine and synthetic biology.

"Cellular processes are complex and constantly change depending on when and where in the cell they occur. Our new chemical tool with light switches will make it easier to control processes in the cell and study how cells function in real time. We can also determine where we make such regulations with a resolution of micrometers within a cell or tissue," says Yaowen Wu, professor in the Department of Chemistry at Umeå University.

The intricate choreography of what happens in a cell is based on the precise distribution and interaction of proteins over time and space. Controlling protein or gene function is a cornerstone of modern biological research.

However, traditional genetic techniques such as CRISPR-Cas9 often operate on a longer time scale, which risks causing cells to adapt. In addition, the techniques lack the spatial and temporal precision required to study highly dynamic cellular processes.

To address these challenges, so-called chemo-optogenetic systems have emerged as powerful tools. These systems combine chemical molecules, optics, and genetically modified proteins to precisely control protein activities at specific locations in cells using light-sensitive small molecules. Professor Wu's lab is at the forefront of developing chemo-optogenetic systems.



Jun Zhang, Laura Herzog and Yaowen Wu have found a way to control proteins in living cells. Credit: Shuang Li

Previously, Wu's lab introduced systems based on a type of molecular glue. These work by bringing two proteins close together to change the localization or activity of a protein. The molecular glues are activated or deactivated by light by removing or cleaving a light-sensitive group. Although these tools represented significant advances, they had limitations in their use and insufficient photo- and chemical stability.

In two new publications in the journals *Angewandte Chemie International Edition* and *Chemistry—A European Journal*, researchers in the Wu lab have developed next-generation chemo-optogenetic tools based on photoswitchable molecular glues. These improve on previous systems and overcome limitations.

Through the modified molecular design, these molecular glues can be turned "on" or "off" like a light switch using light of specific wavelengths, allowing for multiple activation cycles where the two different states either promote or inhibit protein function.

"The new modular design enables enormous versatility of the system with adaptable properties and more stability," says Jun Zhang, staff scientist at the Department of Chemistry at Umeå University.

"In our experiments, we were able to demonstrate precise control over several processes in the cell, including protein function and localization, organelle positioning and protein levels," says Laura Herzog, postdoctoral fellow at the Department of Chemistry at Umeå University.

More information: Jun Zhang et al, Modular Photoswitchable Molecular Glues for Chemo-Optogenetic Control of Protein Function in Living Cells, *Angewandte Chemie International Edition* (2025). DOI: 10.1002/anie.202416456

Jun Zhang et al, Visible-Light-Switchable Molecular Glues for Reversible Control of Protein Function, *Chemistry—A European Journal* (2025). DOI: 10.1002/chem.202403808

Provided by Umea University