Lab turns fluorescent tags into cancer killers

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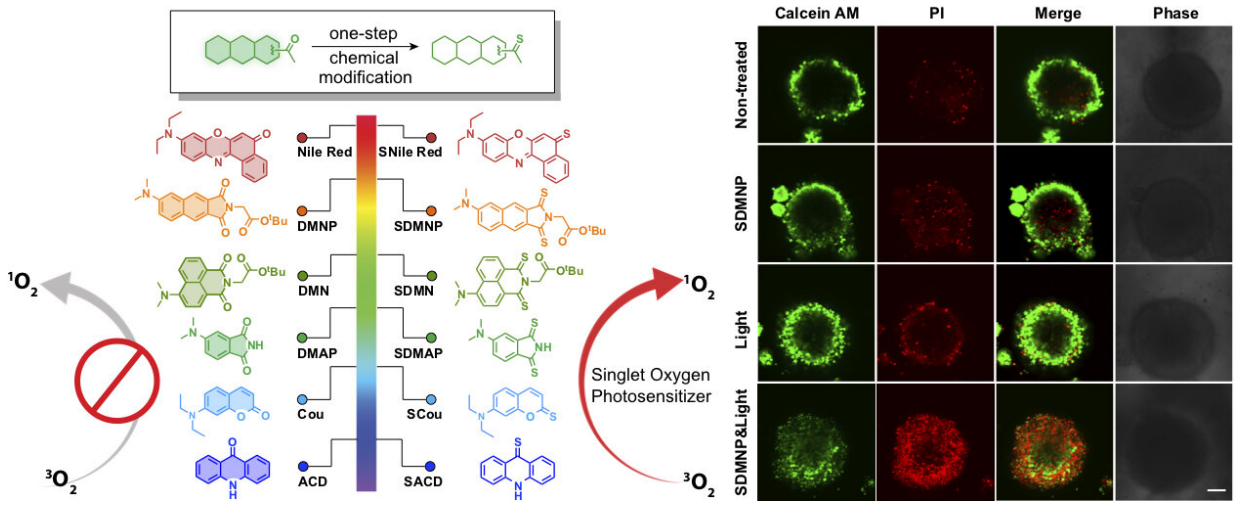

The design of thio-based photosensitizers, at left, by Rice University chemists shows promise for photodynamic cancer therapy, among other applications. One thiocarbonyl substitution -- trading an oxygen atom for a sulfur atom -- of a variety of fluorophores can dramatically enhance their ability to generate reactive oxygen species that kill cancer cells. At right, images of multicellular tumor spheroids treated with photosensitizers and light (in the bottom row) show how the compounds, when excited by light, damage the cells. Credit: Xiao Lab/Rice University

A Rice University lab's project to make better fluorescent tags has turned into a method to kill tumors. Switching one atom in the tag does the trick.

Rice chemist Han Xiao and his colleagues found that replacing a single oxygen atom with a sulfur atom in a common fluorophore turns it into a photosensitizing molecule. When exposed to light, the molecule generated reactive oxygen species (ROS) that destroyed breast cancer cells in the lab.

The study led by co-lead authors Juan Tang and Lushun Wang, both Rice postdoctoral researchers, appears in the Royal Society of Chemistry flagship journal *Chemical Science*.

This method of photodynamic therapy is already in use, as light-triggered molecules are known to generate cytotoxic ROS. Most current photosensitizers require the incorporation of heavy atoms, but they are difficult and costly to synthesize and remain toxic in the dark, potentially damaging healthy cells, Xiao said.

The Rice lab's one-step compounds have no heavy atoms, yield a high ratio of ROS when triggered and shut off when the light is turned off. The lab's various thio-based fluorophores absorb light in visible to near-infrared wavelengths that penetrate up to 5 millimeters into tissues.

"This work comes through our previous study to make better fluorogenic dyes," Xiao said. "That was a totally new discovery, but once we went deeper into the mechanism, we found that our thio-based fluorophores can lead to a dramatic generation of singlet oxygen when excited with light. This is the real mediator."

For testing, the researchers combined their photosensitizers with trastuzumab, an antibody used to target and treat early and advanced breast cancer. The combination showed "robust cytotoxicity" against HER2-positive (cancerous) cell lines but almost no activity against HER2-negative cells.

Xiao said the experiments showed their photosensitizers targeted both monolayer cancer cells and multicellular tumor spheroids. "We think a big application for this photosensitizer will be skin cancers," he said. "It should be easy for light to penetrate basal cell carcinomas on the surface."

The researchers noted solar cells, photocatalytic applications and organic chemistry may benefit from their photosensitizers.

More information: Juan Tang et al, Single-atom replacement as a general approach towards visible-light/near-infrared heavy-atom-free photosensitizers for photodynamic therapy, *Chemical Science* (2020). DOI: 10.1039/d0sc02286a

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