New 'stealth' polymer a promising alternative for delivering drugs around the body

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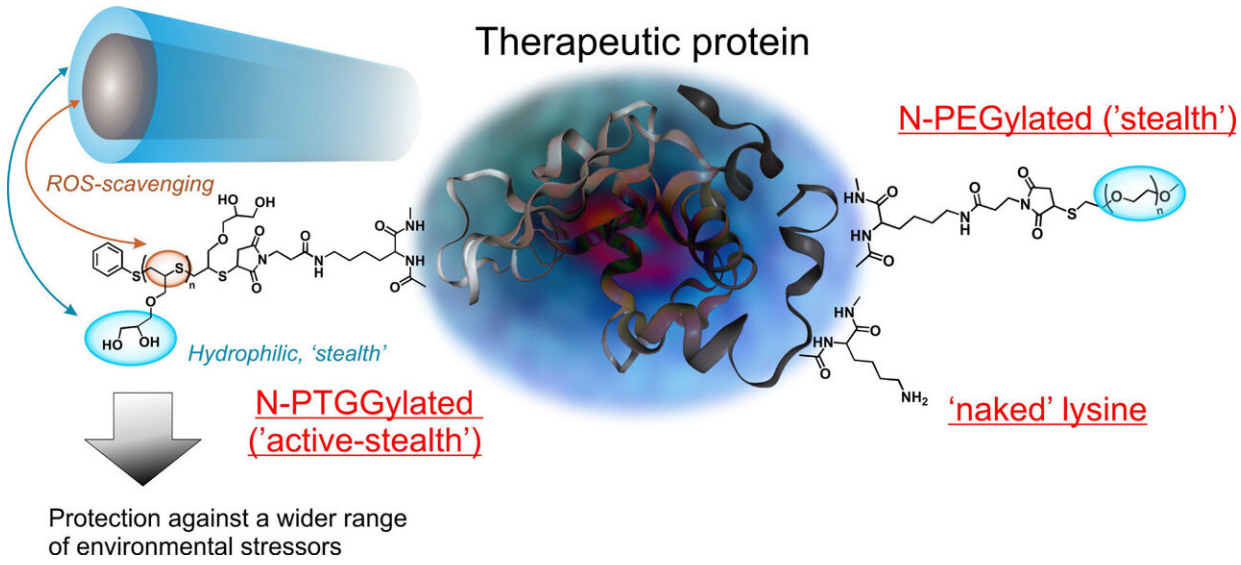

PTGG (Left) Thioethers Allow for Protection against Oxidants (ROS), while Its Hydrophilic Glycerols Provide a 'Stealth' Behavior (Lower Immunogenicity, Higher Stability against Degradation, and Denaturation) Similar to or Better Than PEG (Right). Credit: *Journal of the American Chemical Society* (2022). DOI: 10.1021/jacs.2c09232

Researchers have developed a novel synthetic substance that has the potential to be a more effective and safer way of delivering drugs around the body.

Currently, polyethylene glycol (PEG) is the most commonly used

polymer for biomedical applications due to its non-toxicity and high solubility. It has many applications, including coating nanocarriers which ferry pharmaceuticals in a patient's bloodstream.

While PEGs have a vast number of benefits, there are also significant shortcomings. Currently, researchers have concerns over PEG's own immunogenicity, so their tendency to trigger an unwanted immune response against themselves. The widespread use of PEG in COVID-19 vaccines and boosters has led to significantly higher levels of PEG-antibodies found in vaccinated people.

A team of scientists has created a new "active stealth" polymer, called Polythio Glycidyl glycerol (PTGG), which initial data suggests is safer and more effective in drug-delivery.

The study, published in the *Journal of the American Chemical Society* (*JACS*), found PTGG was less likely to be detected by immune systems when traveling around a body compared to PEG. It also enhanced physical stability and protected tissue from oxidative and inflammatory damage.

Lead author, Dr. Farah El Mohtadi from the University of Portsmouth's School of Pharmacy & Biomedical Sciences, said, "PTGG's 'active-stealth' character makes it a highly promising alternative to PEG for delivering drugs, and therapeutic proteins.

"Not only can it effectively avoid detection in the bloodstream, the polymer's advantageous properties can also significantly reduce the need for expensive substances to prevent freeze-damage during storage."

The study's findings have significant implications for the development of more effective and safer drugs and nanocarriers. Further research will be conducted to explore the potential applications of PTGG in clinical

settings.

"On top of the medical application, we also want to explore PTGG's potential use in other areas," added Dr. El Mohtadi.

"These include temporarily uniting the polymer to enzymes and exploring whether they are more effective at breaking down man-made materials, including plastics."

The potential for using the polymer to stabilize nylon-degrading enzymes will be explored as part of a Ph.D. studentship at the University's Center for Enzyme Innovation (CEI), a project supervised by Professor Andy Pickford (the CEI Director), Dr. El Mohtadi and Dr. Bruce Lichtenstein.

CEI scientists have already developed enzyme technology to reduce single use plastics, including PET, to their chemical building blocks, leading to safe and energy efficient recycling. Now they have set their sights on creating a similar process for polyester textiles, and for this project targeting nylon.

Professor Andy Pickford said, "In an industrial setting, plastic-degrading enzymes must operate under challenging conditions such as high temperature, so we are excited to see whether attaching PTGG to them can enhance their performance."

More information: Richard d'Arcy et al, A Reactive Oxygen Species-Scavenging 'Stealth' Polymer, Poly(thioglycidyl glycerol), Outperforms Poly(ethylene glycol) in Protein Conjugates and Nanocarriers and Enhances Protein Stability to Environmental and Biological Stressors, *Journal of the American Chemical Society* (2022). DOI: 10.1021/jacs.2c09232

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